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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:53:55 ON 13 JAN 2003
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STRUCTURE FILE UPDATES:   12 JAN 2003  HIGHEST RN 478784-40-6
DICTIONARY FILE UPDATES:  12 JAN 2003  HIGHEST RN 478784-40-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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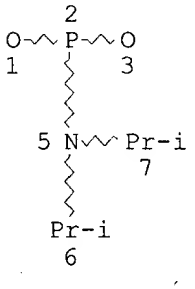


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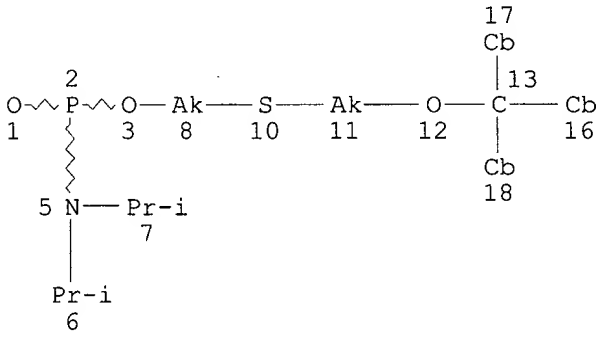

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

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DEFAULT ECLEVEL IS LIMITED

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L34 4 SEA FILE=REGISTRY ABB=ON PLU=ON L32 NOT B/ELS

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 13 Jan 2003 VOL 138 ISS 3
FILE LAST UPDATED: 12 Jan 2003 (20030112/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d l85 bib abs hitstr retable tot

L85 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **2002:716440** HCAPLUS
DN **137:227613**
TI Nucleic acid labeling compounds
IN **McGall, Glenn**; Barone, Anthony D.
PA **Affymetrix, Inc., USA**
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002072779	A2	20020919	WO 2002-US7584	20020312
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002182625	A1	20021205	US 2002-97113	20020312

PRAI US 2001-275202P P 20010312
OS MARPAT 137:227613
AB The present invention relates to nucleic acid labeling compds. More specifically, the invention provides compds. contg. a detectable moiety. The invention also provides methods of making these compds. It further provides methods of attaching the compds. to a nucleic acid. The nucleic acid labeling compds. or the present invention are effectively incorporated into a nucleic acids to provide readily detectable compns. that are useful for genetic anal. technologies. These compds. and the detectable compns. can aid, for example, in the monitoring of gene expression and the detection and screening of mutations and polymorphisms. Thus, the compds. of the invention are suitable for enzymic incorporation into nucleic acids. Furthermore, the nucleic acids to which the labeling compd. are attached maintain their ability to **bind** to a probe, such as, for example a complementary nucleic acid. The present invention provides nucleic acid labeling compds. that are capable of being enzymically incorporated into a nucleic acid. The nucleic acids to which the compds. are attached maintain their ability to **bind** to a complementary nucleic acid sequence. The compds. are synthesized by condensing a heterocyclic deriv. with a cyclic group (e.g. a ribofuranose deriv.).

L85 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:123027 HCAPLUS
DN 136:179591
TI Oligonucleotides containing pyrazolo[3,4-d]pyrimidine analogs of purin-2,6-diamine and their uses as probes and primers
IN Seela, Frank; Bergmann, Frank; Von der Eltz, Herbert; Heindl, Dieter; Seidel, Christoph; Becher, Georg
PA Roche Diagnostics G.m.b.H., Germany; F. Hoffmann-La Roche A.-G.
SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002012263	A1	20020214	WO 2001-EP8850	20010731
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	AU 2001078517	A5	20020218	AU 2001-78517	20010731
PRAI	EP 2000-116816	A	20000803		
	EP 2001-109438	A	20010424		
	WO 2001-EP8850	W	20010731		

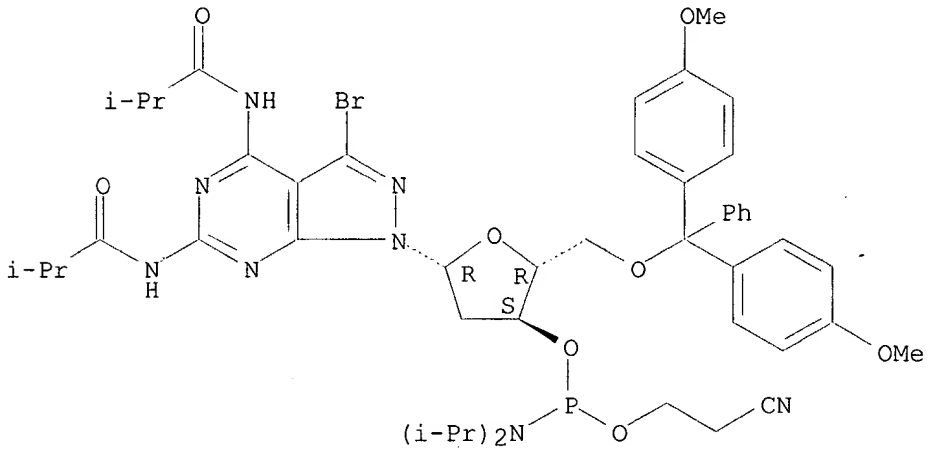
OS MARPAT 136:179591
AB The present invention is in the field of nucleic acid binding compds. comprising 7-substituted 7-deaza-8-aza-2,6-diaminopurine bases, compds. useful for the prepn. of such compds., various uses thereof, and methods for the detn. of nucleic acids using said compds. in the field of diagnostics. Thus, an oligonucleotide having incorporated a 7-iodo- or 7-bromo-8-aza-7-deaza-2,6-diaminopurine in place of an adenine residue shows an unexpected increase in the melting temp. This result is in contrast to the behavior of 5-halogen-substituted pyrimidines. This effect can be obsd. for parallel as well as for antiparallel duplexes. It is hypothesized that similar results would be obtained with 8-aza-7-deaza-2,6-diaminopurines with other hydrophobic or electron-withdrawing groups at the 7-position. The 7-position allows the substituents to extend into the major groove of the DNA where they find enough space and do not disturb the DNA double helix.
IT **356038-36-3P 356038-38-5P 359436-18-3P**
359436-25-2P 359436-26-3P 398117-37-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(oligonucleotides contg. pyrazolo[3,4-d]pyrimidine analogs of purin-2,6-diamine and their uses as probes and primers)

RN 356038-36-3 HCAPLUS

CN Propanamide, N,N'-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-3-bromo-1H-pyrazolo[3,4-d]pyrimidine-4,6-diyl]bis[2-methyl- (9CI) (CA INDEX NAME)

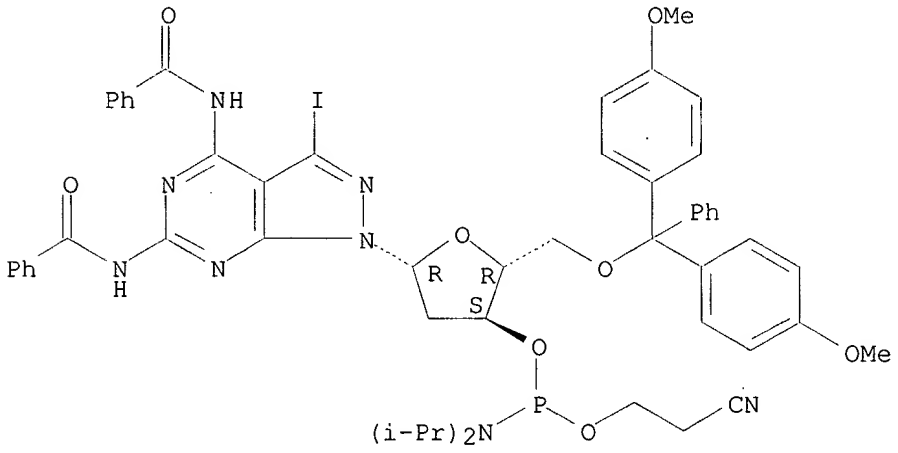
Absolute stereochemistry.



RN 356038-38-5 HCAPLUS

CN Benzamide, N,N'-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-3-iodo-1H-pyrazolo[3,4-d]pyrimidine-4,6-diyl]bis- (9CI) (CA INDEX NAME)

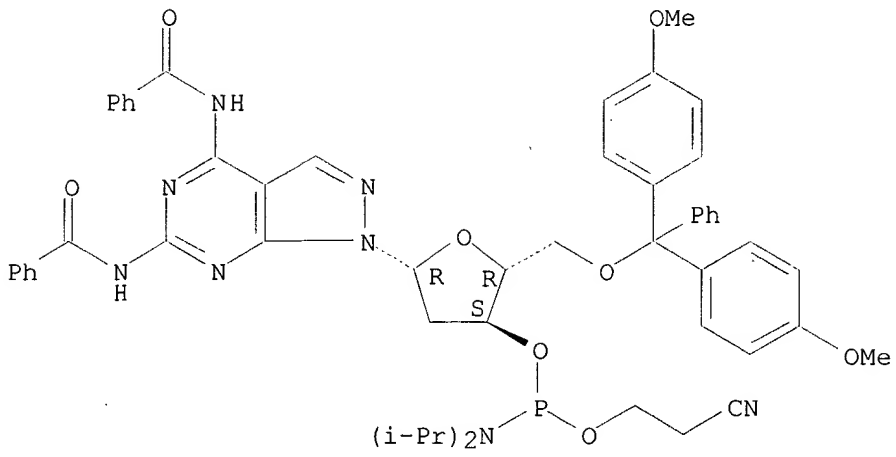
Absolute stereochemistry.



RN 359436-18-3 HCAPLUS

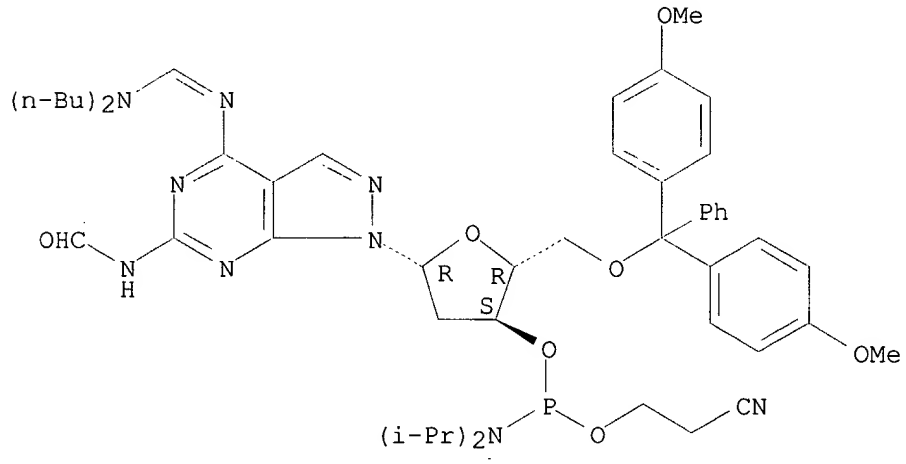
CN Benzamide, N,N'-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-1H-pyrazolo[3,4-d]pyrimidine-4,6-diyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



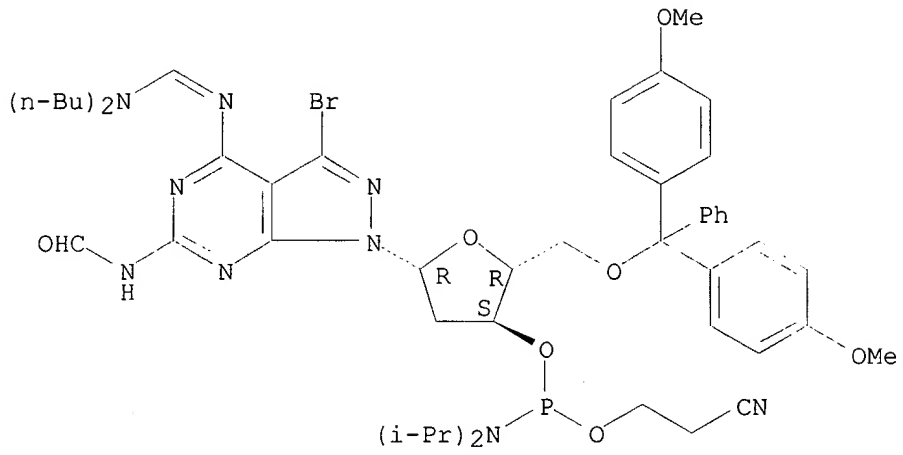
RN 359436-25-2 HCAPLUS
CN Formamide, N-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-4-[[(dibutylamino)methylene]amino]-1H-pyrazolo[3,4-d]pyrimidin-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



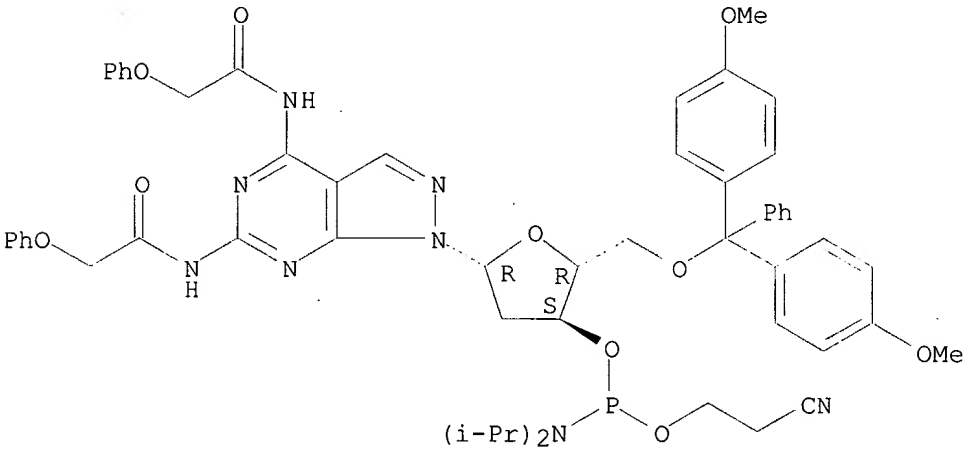
RN 359436-26-3 HCAPLUS
CN Formamide, N-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-3-bromo-4-[[(dibutylamino)methylene]amino]-1H-pyrazolo[3,4-d]pyrimidin-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 398117-37-8 HCAPLUS
CN Acetamide, N,N'-[1-[5-O-[bis(4-methoxyphenyl)phenylmethyl]-3-O-[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]-2-deoxy-.beta.-D-erythro-pentofuranosyl]-1H-pyrazolo[3,4-d]pyrimidine-4,6-diyl]bis[2-phenoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

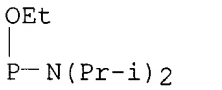
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Balow, G	1998	26	3350	NUCLEIC ACIDS RESEAR	HCAPLUS
Epigenomics Gmbh	1999			DE 19823454 A	HCAPLUS
Epoch Pharmaceuticals I	1999			WO 9951775 A	HCAPLUS
Garaeva, L	1991	10	1295	NUCLEOSIDES NUCLEOTI	HCAPLUS
Microprobe Corp	1990			WO 9003370 A	HCAPLUS
Oertel, F	1992		1165	LIEBIGS ANN CHEM	HCAPLUS
Petrie, C	1991	2	441	BIOCONJUGATE CHEMIST	HCAPLUS
Ramzaeva, N	1999	18	1439	NUCLEOSIDES & NUCLEO	HCAPLUS
Seela, F	1997	16	963	NUCLEOSIDES & NUCLEO	HCAPLUS
Seela, F	1999	18	1399	NUCLEOSIDES & NUCLEO	HCAPLUS

L85 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:741492 HCAPLUS
DN 135:283940

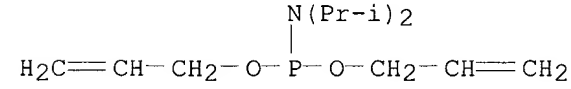
TI Method for synthesizing a specific, surface-bound polymer uniformly over an element of a molecular array using stepwise synthesis with reagents delivered in drops
IN Earhart, Jonathan P.; Perbost, Michel G. M.
PA Agilent Technologies Inc., USA
SO U.S., 28 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6300137	B1	20011009	US 1999-300873	19990428
	US 2002034830	A1	20020321	US 2001-972256	20011005
PRAI	US 1999-300873	A1	19990428		

OS MARPAT 135:283940
AB A method for specifically and uniformly synthesizing desired polymers within mol. array elements. Droplets contg. a reactive monomer are successively applied to the elements of a mol. array in order to synthesize a substrate-bound polymer. Application of an initial droplet, having a first vol., defines the position and size of a mol. array element. Subsequent droplets are applied, to add successive reactive monomers to growing nascent polymers within the mol. array element, with covering vols. so that, even when application of the subsequent droplets is misregistered, the entire surfaces of the elements of the mol. array are exposed to the subsequently applied droplets. Following application of initial droplets, the surface of the mol. array is exposed to a soln. contg. a very efficient capping agent in order to chem. cap any unreacted nascent growing polymers and any unreacted substrate mols.
IT **42053-26-9 126429-21-8**, Diallyl-diisopropyl phosphoramidite
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(capping agent; method for synthesizing specific, surface-bound polymer uniformly over element of mol. array using stepwise synthesis with reagents delivered in drops)
RN 42053-26-9 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 126429-21-8 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, di-2-propenyl ester (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Coolidge	1995			US 5464759	HCAPLUS
Fodor	1995			US 5445934	HCAPLUS
Fodor	1999			US 5925525	HCAPLUS

Pease	1994	91	5022	Proc Natl Acad Sci U	HCAPLUS
Pease	1994	91	5022	Proc Natl Acad Sci U	HCAPLUS
Ravikumar	1996			US 5510476	HCAPLUS
Vargeese	1998			WO 9816540	HCAPLUS
Weiler	1996	243	218	Anal Biochem	HCAPLUS
Weiler	1996	243	218	Anal Biochem	HCAPLUS

L85 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:449217** HCAPLUS
DN **135:56873**
TI Template-specific termination in PCR using non-extensible blocking oligonucleotides hybridizing to homologs of the target sequence
IN Liles, Mark R.; Goodman, Robert M.
PA Wisconsin Alumni Research Foundation, USA
SO U.S., 21 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6248567	B1	20010619	US 2000-557248	20000424
WO 2001081630	A2	20011101	WO 2001-US12524	20010416
WO 2001081630	A3	20020822		

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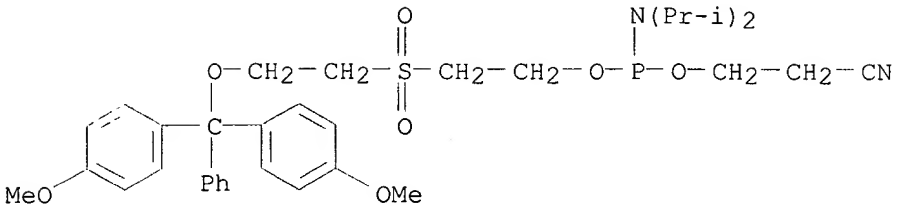
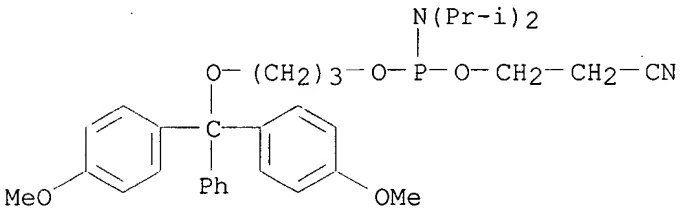
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-557248 A 20000424
AB A method of selectively inhibiting the amplification of a specific DNA template during a polymerase chain reaction (PCR) is described. In particular, the method is useful when the sequences of the desired and undesired DNA templates are similar. A set of universal primers binds to both the desired and undesired DNA templates during a PCR, resulting in the amplification of their DNA sequences. The method targets the undesired DNA template with three sets of oligonucleotide primers, one set of which is terminally modified to both prevent primer extension and increase the primer-template binding affinity. The result of these terminal modifications is the specific inhibition of the PCR amplification of the undesired DNA template, allowing the preferential amplification of the desired DNA templates. Use of the method to selectively amplify Bacillus cereus 16S rRNA genes from genomic library in Escherichia coli is demonstrated.
IT **108783-02-4 110894-23-0**
RL: MOA (Modifier or additive use); USES (Uses)
(as blocking group on oligonucleotides; template-specific termination in PCR using non-extensible blocking oligonucleotides hybridizing to homologs of target sequence)
RN 108783-02-4 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-[[2-[bis(4-methoxyphenyl)phenylmethoxy]ethyl]sulfonyl]ethyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)



RN 110894-23-0 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 3-[bis(4-methoxyphenyl)phenylmethoxy]propyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bunn	1993			US 5213961	HCAPLUS
Carson	1998			US 5747251	HCAPLUS
Chenchik	1998			US 5759822	HCAPLUS
Li, H	1988	335	414	Nature	HCAPLUS
Mullis	1987			US 4683195	HCAPLUS
Mullis	1987			US 4683202	HCAPLUS
Wang	1993			US 5219727	HCAPLUS

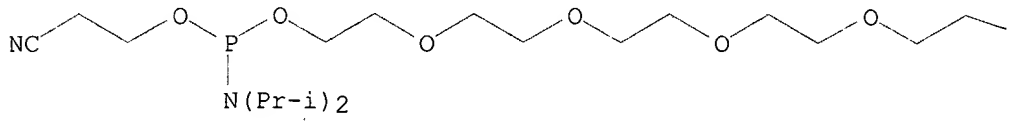
L85 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:303883 HCAPLUS
DN 135:242450
TI Photolithographic synthesis of high-density oligonucleotide arrays
AU **McGall, Glenn H.**; Fidanza, Jacqueline A.
CS **Affymetrix Inc., Santa Clara, CA, USA**
SO Methods in Molecular Biology (Totowa, NJ, United States) (2001), 170(DNA Arrays), 71-101
CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal
LA English
OS CASREACT 135:242450
AB High-d. polynucleotide probe arrays provide a massively parallel approach to genetic sequence anal. that is having a major impact on bio-medical research and clin. diagnostics. We describe methods for the synthesis of photolabile MeNPOC nucleoside phosphoramidite building blocks for std. 3'-5' as well as 5'-3' photolithog. synthesis, and for "modified" 2'-O-Me and 2,6-diaminopurine nucleosides that can be used to improve hybridization affinities of AT-probe sequences. We also outline the photolithog. synthesis method, general protocols for detg. photochem. deprotection rates and yields for oligonucleotide synthesis based on surface fluorescence, as well as procedures based on hybridization for comparing the array performance characteristics of new chemistries and protocols.
IT **125607-09-2**

RL: RCT (Reactant); RACT (Reactant or reagent)
(photolithog. synthesis of high-d. oligonucleotide arrays)

RN 125607-09-2 HCAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 2-cyanoethyl 19,19-bis(4-methoxyphenyl)-19-phenyl-3,6,9,12,15,18-hexaoxanonadec-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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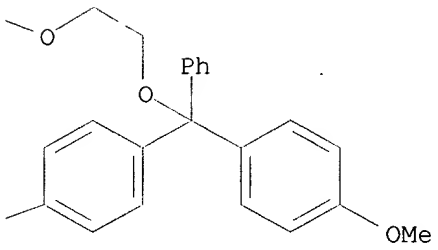
PAGE 1-B



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Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1999	21	1	Nat Genet	
Barone, A	1984	12	4051	Nucleic Acids Res	HCAPLUS
Beecher, J	1997	76	597	Am Chem Soc Div Poly	HCAPLUS
Broude, N	1994	91	3072	Proc Natl Acad Sci	HCAPLUS
Chee, M	1996	274	610	Science	HCAPLUS
Cheong, C	1988	16	5115	Nucleic Acids Res	HCAPLUS
Chollet, A	1985	26	37	Chem.Scripta	
Chollet, A	1994	26	37	Chem Scripta	
Fidanza, J	1999	18	1293	Nucleosides Nucleoti	HCAPLUS
Fodor, S	1991	251	767	Science	HCAPLUS
Gaffney, B	1984	40	3	Tetrahedron	HCAPLUS
Giegrich, H	1998	17	1987	Nucleosides Nucleoti	HCAPLUS
Gryaznov, S	1994	35	2489	Tetrahedron Lett	HCAPLUS
Gunderson, K	1998	8	1142	Genome Res	HCAPLUS
Hasan, A	1997	53	4247	Tetrahedron	HCAPLUS
Hoheisel, J	1990	274	103	FEBS Lett	HCAPLUS
Howard, F	1984	23	6723	Biochemistry	HCAPLUS
Inoue, H	1987	15	6131	Nucleic Acids Res	HCAPLUS
Kozal, M	1996	7	753	Nat Med	
Lipshutz, R	1999	21	20	Nat Genet	
Lockhart, D	1996	14	1675	Nat Biotechnol	HCAPLUS
Majlessi, M	1998	26	2224	Nucleic Acids Res	HCAPLUS
Maskos, U	1993	21	4663	Nucleic Acids Res	HCAPLUS
McGall, G	1997		2.1	Biochip Arrays and I	
McGall, G	1997	119	5081	J Am Chem Soc	HCAPLUS
McGall, G	1996	93	13555	Proc Natl Acad Sci	HCAPLUS

Pease, A	1994	91	5022	Proc Natl Acad Sci	HCAPLUS
Pirrung, M	1994	4	1345	Bioorgan Med Chem Le	HCAPLUS
Pirrung, M	1995	60	1116	J Org Chem	HCAPLUS
Pirrung, M	1995	60	6270	J Org Chem	HCAPLUS
Pirrung, M	1998	63	241	J Org Chem	HCAPLUS
Prosnyak, M	1994	21	490	Genomics	HCAPLUS
van Boom, J	1984		153	Oligonucleotide Synt	
Wallraff, G	1997	27	22	Chemtech	HCAPLUS

L85 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:78405** HCAPLUS
DN **134:126778**
TI Even length proportional amplification of nucleic acids
IN Lockhart, David; Lai, Chao-Qiang; Gunderson, Kevin
PA **Affymetrix, Inc., USA**
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001007464	A1	20010201	WO 2000-US19841	20000721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6495320	B1	20021217	US 1999-358664	19990721
PRAI US 1999-358664	A	19990721		

AB The present invention addresses the issue of amplifying of DNA or RNA in an unbiased fashion, thus providing the accurate detn. of gene expression in even a single cell or a small amt. of tissue. Even length proportional amplification of nucleic acids can increase the amt. of nucleic acids while preserving the relative abundance of the individual nucleic acid species, or portions thereof, in the original sample. The cDNA target that is synthesized from mRNA is randomly digested into equal or roughly equal length fragments; then an adapter is attached at both ends of these fragments, and subsequently the fragments amplified by PCR. Random digestion into equal length fragments facilitates unbiased PCR amplification of the original mRNA population, and is achieved using 1,10-phenanthroline-copper as a cutter. An even length proportionally amplified nucleic acid prepn. may be analyzed in a gene expression monitoring system, preferably involving a nucleic acid probe array.

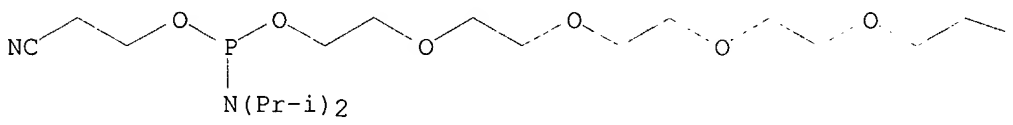
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Avila	1993	31	2421	J of Clinical Microb	HCAPLUS
Chen	1986	83	7147	Proc Natl Acad Sci	HCAPLUS
Chen	1993	90	4206	Proc Natl Acad Sci U	HCAPLUS
Goller	1998	16	2945	Glutaredoxin is a Di	HCAPLUS
Kuwabara	1987	26	7234	Biochemistry	HCAPLUS
Ramesh	1996	260	22	J Molecular Biology	HCAPLUS

L85 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:776207 HCAPLUS
DN 134:71834
TI A novel phosphoramidite method for automated synthesis of oligonucleotides

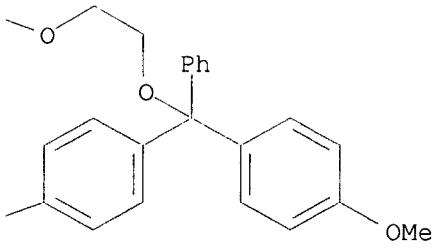
on glass supports for biosensor development
AU Sojka, Bernd; Piunno, Paul A. E.; Wust, Christopher C.; Krull, Ulrich J.
CS Chemical Sensors Group, Department of Chemistry, University of Toronto at Mississauga, Mississauga, ON, L5L 1C6, Can.
SO Applied Biochemistry and Biotechnology (2000), 89(1), 85-103
CODEN: ABIBDL; ISSN: 0273-2289
PB Humana Press Inc.
DT Journal
LA English
AB Two protocols for functionalization of glass supports with hexaethylene glycol (HEG)-linked oligonucleotides were developed. The first method (std. amidite protocol) made use of the 2-cyanoethyl-phosphoramidite deriv. of 4,4'-dimethoxytrityl-protected HEG. This was first coupled to the support by std. solid-phase phosphoramidite chem. followed by extension with a thymidylic acid icosanucleotide. Stepwise addn. of the linker phosphoramidite graduated at 1% (relative to the total sites available) per step at 50.degree.C resulted in an optimal yield of immobilized oligonucleotides at a d. of 2.24 .times. 1010 strands/mm2. This obsd. loading max. lies well below the theor. max. loading owing to **non-specific** adsorption of HEG on the glass and subsequent blocking of reactive sites. Surface loadings as high as 3.73 .times. 1010/mm2 and of excellent sequence quality were achieved with a reverse amidite protocol. The support was first modified into a 2-cyanoethyl-N,N-diisopropylphosphoramidite analog followed by coupling with 4,4'-dimethoxytrityl-protected HEG. This protocol is conveniently available when using a conventional DNA synthesizer. The reverse amidite protocol allowed for control of the surface loading at values suitable for subsequent anal. applications that make use of immobilized oligonucleotides as probes for selective hybridization of sample nucleic acids of unknown sequence and concn.
IT **125607-09-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(phosphoramidite method for automated synthesis of oligonucleotides on glass supports for biosensor development)
RN 125607-09-2 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-cyanoethyl 19,19-bis(4-methoxyphenyl)-19-phenyl-3,6,9,12,15,18-hexaoxanonadec-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A



MeO

PAGE 1-B



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Abel, A	1996	68	2905	Anal Chem	HCAPLUS
Chrisey, L	1996	24	3040	Nucleic Acids Res	HCAPLUS
Cohen, G	1997	25	911	Nucleic Acids Res	HCAPLUS
Guo, Z	1994	22	5456	Nucleic Acids Res	HCAPLUS
Hudson, R	1993	115	2119	J Amer Chem Soc	HCAPLUS
Maskos, U	1992	20	1679	Nucleic Acids Res	HCAPLUS
Matthews, J	1988	169	1	Anal Biochem	HCAPLUS
McGall, G	1996	119	5081	J Amer Chem Soc	
Piunno, P	1995	67	2635	Anal Chim	HCAPLUS
Polushin, N	1994	22	639	Nucleic Acids Res	HCAPLUS
Rajur, B	1997	62	523	J Org Chem	
Shchepinov, M	1997	25	1155	Nucleic Acids Res	HCAPLUS
Smith, L	1995	12	33	Gen Anal	
Uddin, A	1997	25	4139	Nucleic Acids Res	HCAPLUS
Zhang, Y	1991	19	3929	Nucleic Acids Res	HCAPLUS

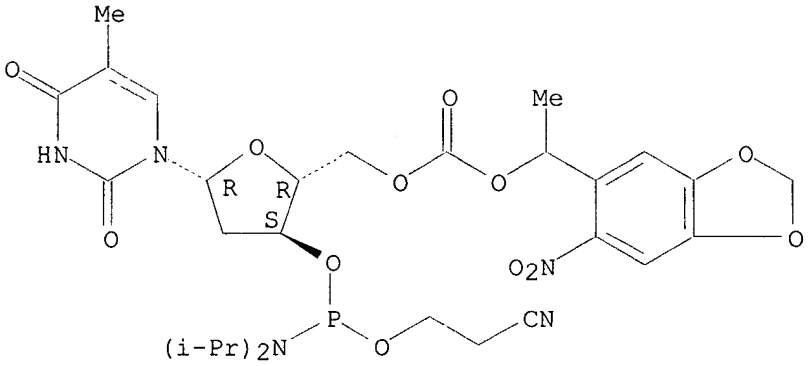
L85 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:632858 HCAPLUS
DN 133:203447
TI Production by quantitative photolithographic synthesis of individually quality checked DNA microarrays
AU Beier, Markus; Hoheisel, Jorg D.
CS Functional Genome Analysis, Deutsches Krebsforschungszentrum, Heidelberg, D-69120, Germany
SO Nucleic Acids Research (2000), 28(4), e11, ii-vi
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB For DNA chip analyses, oligonucleotide quality has immerse consequences for accuracy, sensitivity and dynamic range. The quality of chips produced by photolithog. in situ synthesis depends critically on the efficiency of photo-deprotection. By means of base-assisted enhancement of this process using 5'-[2-(2-nitrophenyl)-propyloxycarbonyl]-2'-deoxynucleoside phosphoramidites, synthesis yields improved by at least 12% per condensation compared to current chemistries. Thus, the eventual total yield of full-length oligonucleotide is increased more than 10-fold in the case of 20mers. Furthermore, the quality of every individual array position was checked quant. after synthesis. Subsequently, the quality tested chips were used in successive hybridization expts.
IT **159873-67-3 159873-69-5 159873-70-8**
289885-25-2 289885-26-3 289885-27-4
289885-28-5 289885-29-6
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prodn. by quant. photolithog. synthesis of individually quality

checked DNA microarrays for)

RN 159873-67-3 HCAPLUS

CN Thymidine, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[1-(6-nitro-1,3-benzodioxol-5-yl)ethyl carbonate] (9CI) (CA INDEX NAME)

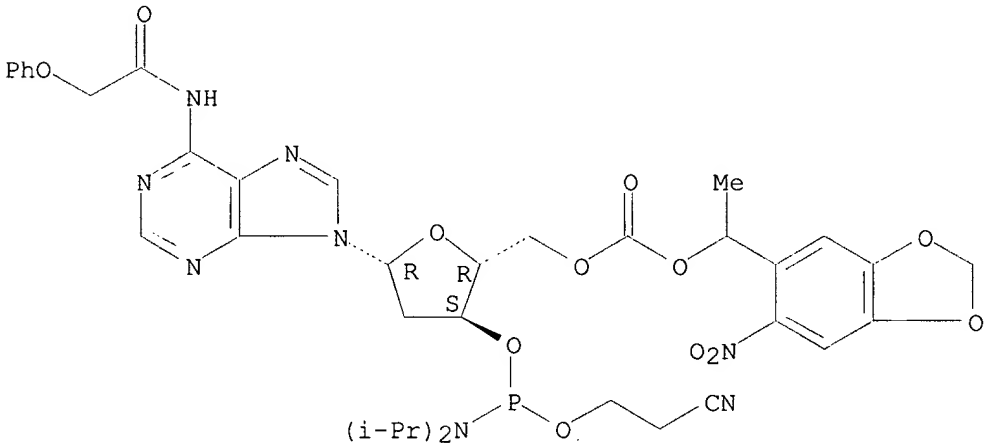
Absolute stereochemistry.



RN 159873-69-5 HCAPLUS

CN Adenosine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[1-(6-nitro-1,3-benzodioxol-5-yl)ethyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

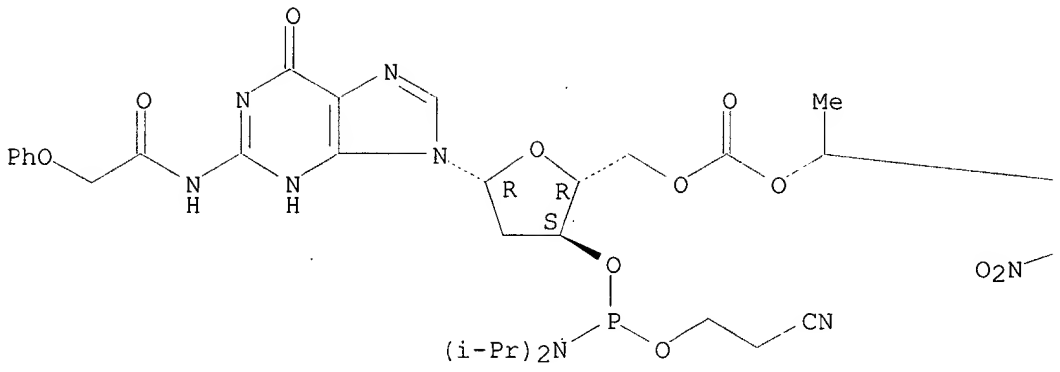


RN 159873-70-8 HCAPLUS

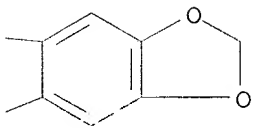
CN Guanosine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[1-(6-nitro-1,3-benzodioxol-5-yl)ethyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

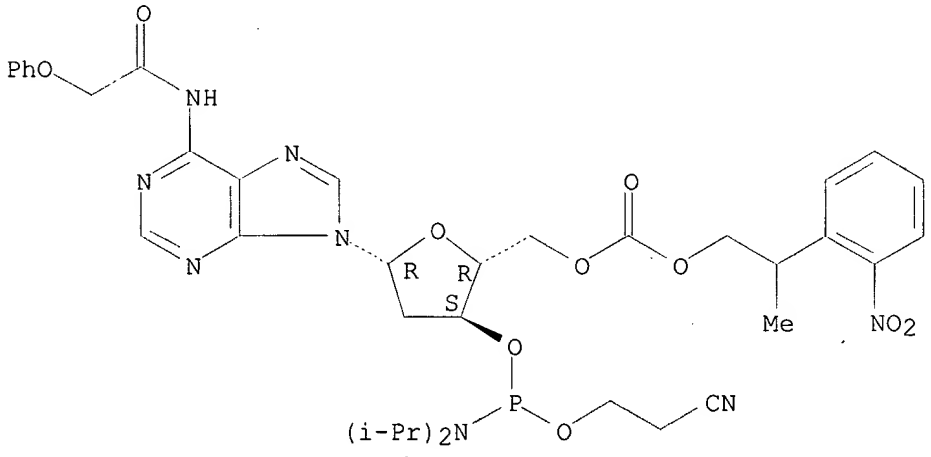


PAGE 1-B



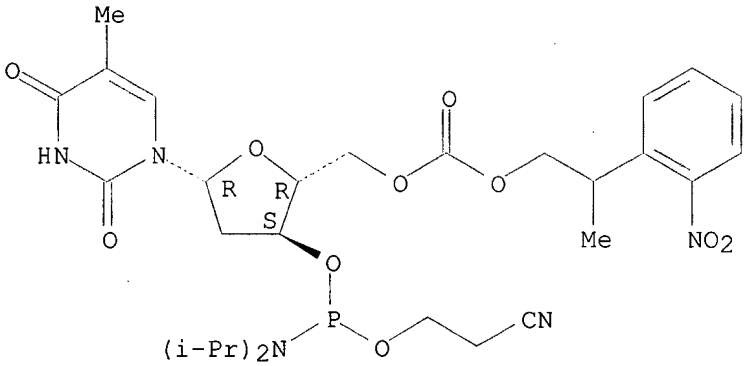
RN 289885-25-2 HCAPLUS
CN Adenosine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[2-(2-nitrophenyl)propyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



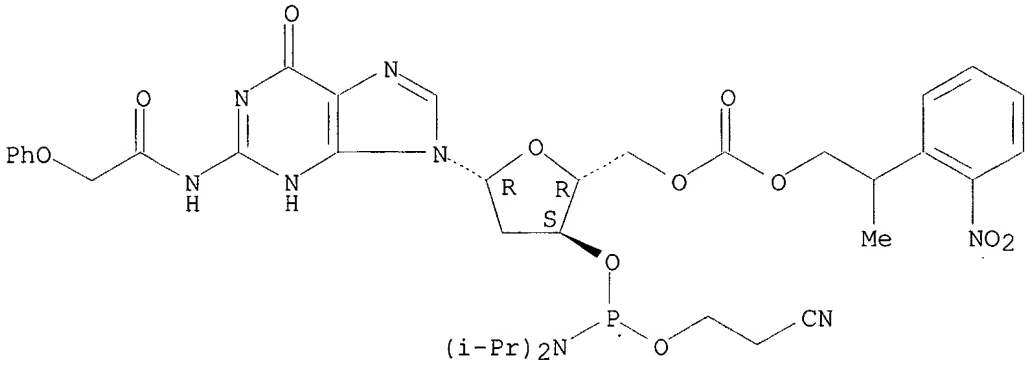
RN 289885-26-3 HCAPLUS
CN Thymidine, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[2-(2-nitrophenyl)propyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



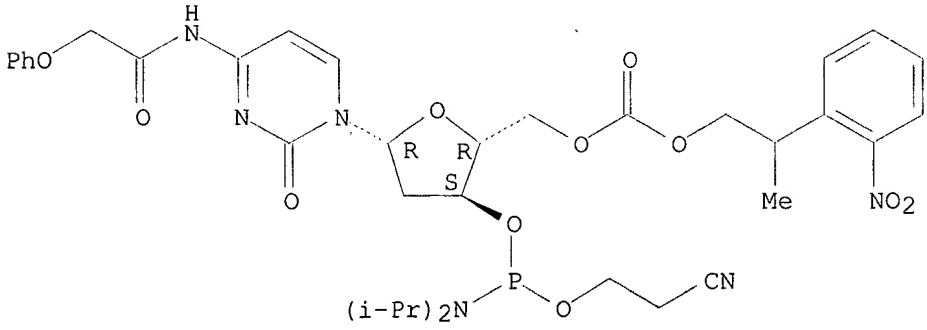
RN 289885-27-4 HCAPLUS
CN Guanosine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[2-(2-nitrophenyl)propyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289885-28-5 HCAPLUS
CN Cytidine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[2-(2-nitrophenyl)propyl carbonate] (9CI) (CA INDEX NAME)

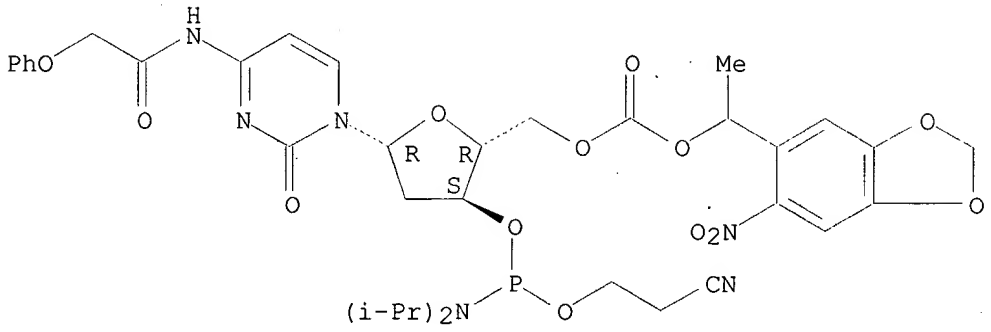
Absolute stereochemistry.



RN 289885-29-6 HCAPLUS
CN Cytidine, 2'-deoxy-N-(phenoxyacetyl)-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[1-(6-nitro-1,3-benzodioxol-5-

yl)ethyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



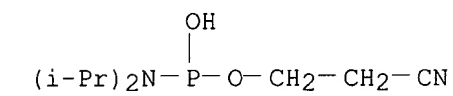
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Ahrendt, S	1999	96	7382	Proc Natl Acad Sci U	HCAPLUS
Beier, M	1999	27	1970	Nucleic Acids Res	HCAPLUS
Bulyk, M	1999	17	573	Nature Biotechnol	HCAPLUS
Cho, R	1998	2	65	Mol Cell	HCAPLUS
Fodor, S	1993	364	555	Nature	MEDLINE
Giegrich, H	1998	17	1987	Nucl Nucl	HCAPLUS
Hasan, A	1997	53	4247	Tetrahedron	HCAPLUS
McGall, G	1997	119	5081	J Org Chem	HCAPLUS
Pease, A	1994	91	5022	Proc Natl Acad Sci U	HCAPLUS
Pirrung, M	1995	60	6270	J Org Chem	HCAPLUS
Pirrung, M	1998	63	241	J Org Chem	HCAPLUS
Ronaghi, M	1998	281	363	Science	HCAPLUS
The Chipping Forecast	1999	21		Nature Genet	
Wang, D	1998	280	1077	Science	HCAPLUS
Winzeler, E	1999	285	901	Science	HCAPLUS

L85 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:573811 HCAPLUS
DN 133:161567
TI Apparatus and method for compound library preparation using an optical modulator
IN Seo, Jeong-sun; Lee, Yoon-sik; Kim, Yong-kweon
PA Macrogen Inc., S. Korea
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000047598	A1	20000817	WO 2000-KR100	20000210
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1180111	A1	20020220	EP 2000-904105	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2002541433 T2 20021203 JP 2000-598516 20000210
PRAI KR 1999-4639 A 19990210
WO 2000-KR100 W 20000210
AB The present invention relates to the provision of compd. libraries, more particularly it provides a compd. library prepn. method using an optical modulator and a compd. library prepn. app. used in the same. Furthermore, the present invention provides a compd. analyzing method using the prepn. method and a compd. analyzing app. used in the same.
IT **133485-25-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(app. and method for compd. library prepn. using an optical modulator)
RN 133485-25-3 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, mono(2-cyanoethyl) ester (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Affymax Technologies N	1992			US 5143854 A	HCAPLUS
Chiron Co	1993			US 5258506 A	HCAPLUS
Joel, M	1992			US 5079600 A	HCAPLUS
Seiko Epson Corp	1997			JP 9159937 A	
Seiko Epson Corp	1997			JP 9236762 A	
Sony Corp	1994			JP 07306368 A	

L85 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:227820** HCAPLUS
DN **132:261363**
TI Methods and compounds for amplifying labeling signals used in a specific **binding** assay for nucleic acid detection
IN **Goldberg, Martin J.**; Yelagalawadi, Govinda Rao S.; Tanimoto, Eugene Yuji; Tran, Huu Minh; Dong, Helin; Lockhart, David J.; **Ryder, Thomas B.**; Warrington, Janet A.; Beecher, Jody
PA **Affymetrix, Inc., USA**
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000018962	A1	20000406	WO 1999-US22584	19990928
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6203989	B1	20010320	US 1999-276774	19990325
EP 999285	A1	20000510	EP 1999-250336	19990922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9962750	A1	20000417	AU 1999-62750	19990928

JP 2000106876 A2 20000418 JP 1999-277610 19990929
US 2001041335 A1 20011115 US 2001-776770 20010206
PRAI US 1998-102577P P 19980930
US 1999-276774 A 19990325
WO 1999-US22584 W 19990928

AB The present invention relates to methods and compds. for amplifying labeling signals used in a specific **binding** assay for nucleic acid detection. The nucleic acid samples contg. the **binding** ligand in the detection assay (such as biotin) can be prepd. by nucleic acid amplification in the presence of biotinylated nucleotides, for example: PCR amplication of plasmid library to form biotinylated cRNA. The nucleic acid targets in the samples, first hybridized to the probe immobilized on a surface, can contact labeled ligand receptor (such as fluorescent streptavidin) through ligand-receptor interaction. The detectable signal of receptor labels can then be enhanced and amplified by adding an amplification compd. comprising a plurality of the **binding** ligands (such as biotinylated anti-streptavidin antibody). An array of different nucleic acid probes immobilized on a surface, each having a defined sequence and location on the surface, may be used in the assays, thus permitting screening and detection of **binding** of large no. of nucleic acids. The invention provides a rapid nucleic acid detection assay with improved specificity and sensitivity.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Gen Trak Inc	1993			WO 9324658 A	HCAPLUS
Kerstens, H	1995	43	347	The Journal of Histo	HCAPLUS
Molecular Devices Corp	1990			WO 9004786 A	
Molecular Diagnostics I	1985			EP 0154884 A	HCAPLUS
Nilsen, T	1996			US 5487973 A	HCAPLUS
Polyprobe Inc	1998			WO 9818488 A	HCAPLUS
Sinai School Medicine	1998			WO 9804745 A	HCAPLUS
Univ Boston	1995			WO 9520320 A	HCAPLUS
Urdea, M	1997			US 5635352 A	HCAPLUS

L85 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:227668 HCAPLUS
DN 132:279476
TI Synthesis of codon randomized nucleic acids
IN Lohse, Peter; Kuimelis, Robert G.
PA Phylos, Inc., USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000018778	A1	20000406	WO 1999-US22436	19990928
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9962704	A1	20000417	AU 1999-62704	19990928

PRAI US 1998-102299P P 19980929
WO 1999-US22436 W 19990928

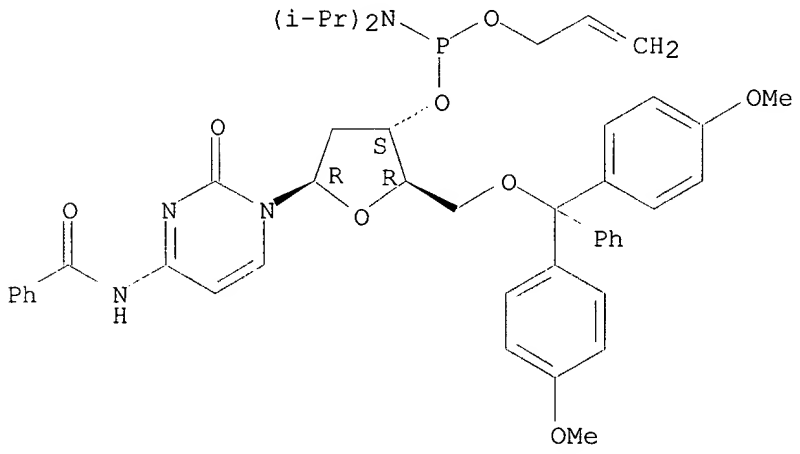
AB A method for generating a selected set of codons is disclosed; the method

includes the steps of: (a) providing a first set of mononucleosides, mononucleotides, dinucleotides, or mixt. thereof, where a subset A of the first set is protected with a protecting group A', and a subset B of the first set is protected with a protecting group B', where A' and B' are orthogonal protecting groups; (b) selectively removing the protecting group A' from subset A; (c) coupling the products of step (b) with a second set of mononucleosides, mononucleotides, dinucleotides, or a mixt. thereof, where the second set is protected with protecting group A'; (d) optionally removing protecting group A' from the products of step (c); (e) optionally coupling the products of step (d) with a third set of mononucleosides, where the third set is protected with protecting group A'; (f) selectively removing the protecting group B' from subset B; (g) coupling the products of step (f) with a fourth set of mononucleosides, mononucleotides, dinucleotides, or a mixt. thereof, where the fourth set is protected with protecting group A' or protecting group B'; (h) optionally selectively removing protecting group B' from the products of step (g); and (i) optionally coupling the products of step (h) with a fifth set of mononucleosides, to yield a selected set of codons.

IT **263136-60-3P 263136-61-4P 263136-64-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of codon randomized nucleic acids)

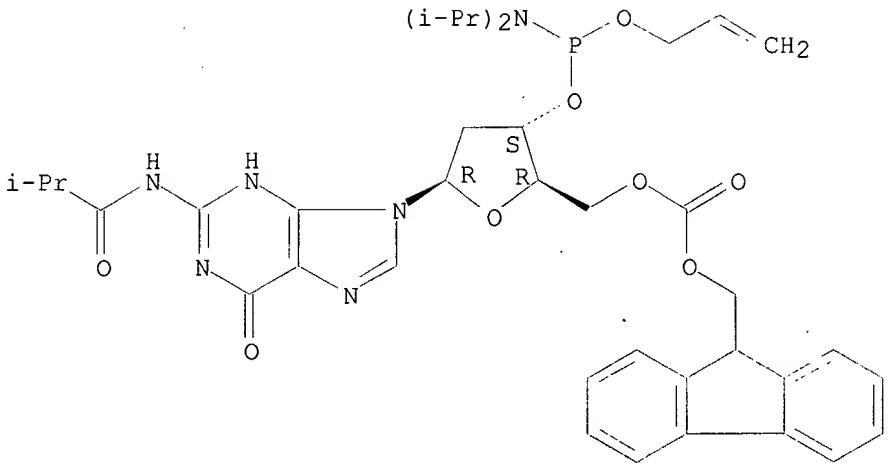
RN 263136-60-3 HCAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-, 3'-[2-propenyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



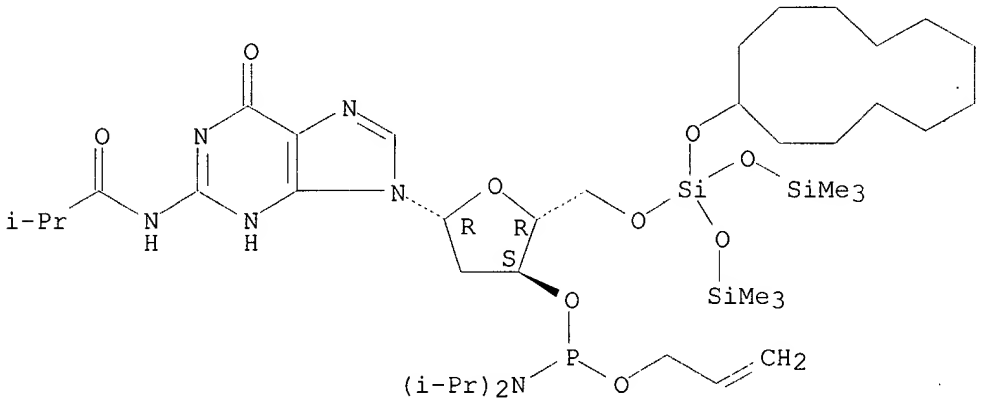
RN 263136-61-4 HCAPLUS
CN Guanosine, 2'-deoxy-N-(2-methyl-1-oxopropyl)-, 5'-(9H-fluoren-9-ylmethyl carbonate) 3'-[2-propenyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 263136-64-7 HCAPLUS
CN Guanosine, 5'-O-[1-(cyclododecyloxy)-3,3,3-trimethyl-1-[(trimethylsilyl)oxy]disiloxanyl]-2'-deoxy-N-(2-methyl-1-oxopropyl)-, 3'-[2-propenyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Scaringe	1999			US 5889136 A	HCAPLUS
Urdea	1997			US 5703218 A	HCAPLUS

L85 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:145072** HCAPLUS
DN **132:176591**
TI Use of pooled probes in multipart arrays for genetic analysis assays
IN Gentalen, Erik; Chee, Mark
PA **Affymetrix, Inc., USA**
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2000011223 A1 20000302 WO 1999-US19069 19990819
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6306643 B1 20011023 US 1998-138958 19980824
CA 2341483 AA 20000302 CA 1999-2341483 19990819
AU 9955778 A1 20000314 AU 1999-55778 19990819
EP 1108062 A1 20010620 EP 1999-942387 19990819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002523064 T2 20020730 JP 2000-566474 19990819
US 2002106663 A1 20020808 US 2001-930536 20010814
PRAI US 1998-138958 A2 19980824
WO 1999-US19069 W 19990819

AB The invention provides arrays of polynucleotide probes having at least one pooled position, a typical array comprises a support having at least three discrete regions, the first bearing a pool of first and second probes, the second baring only the second probe, and the third bearing only the first. A target nucleic acid having segments complementary to both the first and second probes shows stronger normalized **binding** to the first region than to the aggregate of **binding** to the second and third regions due to cooperative **binding** of pooled probes in the first region. The invention provides methods of using such arrays for e.g., linkage anal., sequence anal., and expression monitoring.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Affymax Technologies N	1995			WO 9511995 A1	HCAPLUS
Drmanac	1996			US 5525464 A	HCAPLUS
Drmanac	1997			US 5695940 A	HCAPLUS
Southern	1997			US 5700637 A	HCAPLUS

L85 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:691252 HCAPLUS
DN 131:318549
TI Methods for reducing **non-specific binding** to a nucleic acid probe array by controlled modification of probes or immobilizing surfaces
IN **McGall, Glenn; Goldbert, Martin; Ryder, Thomas B.; Woodman, Steve**
PA **Affymetrix, Inc., USA**
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 9954509 A1 19991028 WO 1999-US8745 19990420 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2326498	AA	19991028	CA 1999-2326498	19990420	<--
AU 9936591	A1	19991108	AU 1999-36591	19990420	<--
EP 1071821	A1	20010131	EP 1999-918749	19990420	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002512045	T2	20020423	JP 2000-544837	19990420	<--
US 2001049108	A1	20011206	US 2001-862571	20010523	<--
PRAI US 1998-63311	A1	19980420	<--		
WO 1999-US8745	W	19990420	<--		

OS MARPAT 131:318549

AB The present invention provides a variety of methods for reducing **non-specific binding** of a target mol. or plurality of target mols. to an array of oligonucleotides. The methods of the present invention include surface modification techniques and oligonucleotide modification techniques. Methods of integrating probe synthesis and surface modification are described. According to one method of the present invention, **non-specific binding** of a target mol. to an array of oligonucleotides is reduced by replacing at least one of: the protecting groups on each of the plurality of oligonucleotides, and the protecting groups on each of the protected regions of the substrate, with a neg. charged phosphate residue. Use of these methods to eliminate background in microarray hybridization is demonstrated.

IT **1303-00-0**, Gallium arsenide, uses **7440-21-3**, Silicon, uses **7440-56-4**, Germanium, uses **9002-84-0** **9003-53-6**, Polystyrene
RL: DEV (Device component use); USES (Uses)
(as substrate for oligonucleotide microarray immobilization; methods for reducing **non-specific binding** to nucleic acid probe array by controlled modification of probes or immobilizing surfaces)

RN 1303-00-0 HCAPLUS
CN Gallium arsenide (GaAs) (8CI, 9CI) (CA INDEX NAME)

Ga≡As

RN 7440-21-3 HCAPLUS
CN Silicon (7CI, 8CI, 9CI) (CA INDEX NAME)

Si

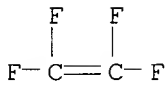
RN 7440-56-4 HCAPLUS
CN Germanium (7CI, 8CI, 9CI) (CA INDEX NAME)

Ge

RN 9002-84-0 HCAPLUS
CN Ethene, tetrafluoro-, homopolymer (9CI) (CA INDEX NAME)

CM 1

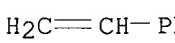
CRN 116-14-3
CMF C2 F4



RN 9003-53-6 HCAPLUS
CN Benzene, ethenyl-, homopolymer (9CI) (CA INDEX NAME)

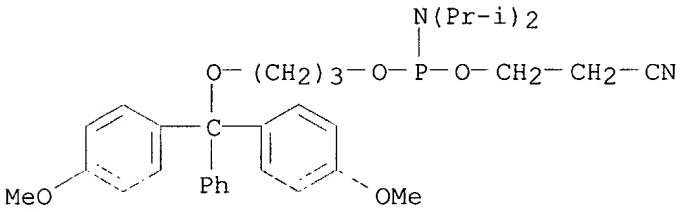
CM 1

CRN 100-42-5
CMF C8 H8



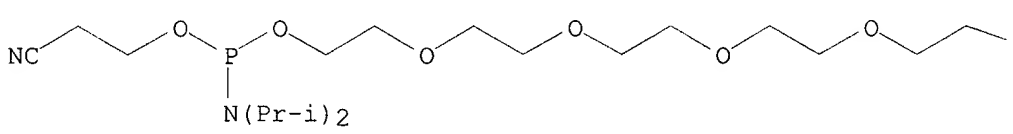
IT **110894-23-0 125607-09-2 247934-62-9**
247934-63-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(for synthesis and immobilization of oligonucleotide microarrays; methods for reducing **non-specific binding** to nucleic acid probe array by controlled modification of probes or immobilizing surfaces)

RN 110894-23-0 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 3-[bis(4-methoxyphenyl)phenylmethoxy]propyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)

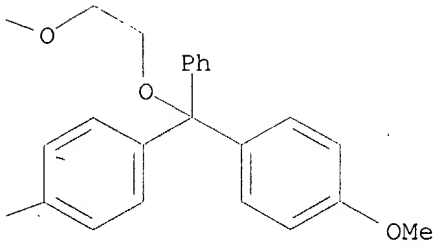


RN 125607-09-2 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-cyanoethyl 19,19-bis(4-methoxyphenyl)-19-phenyl-3,6,9,12,15,18-hexaoxanonadec-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

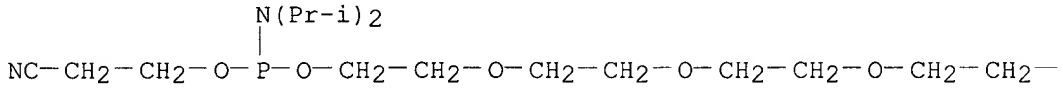


PAGE 1-B

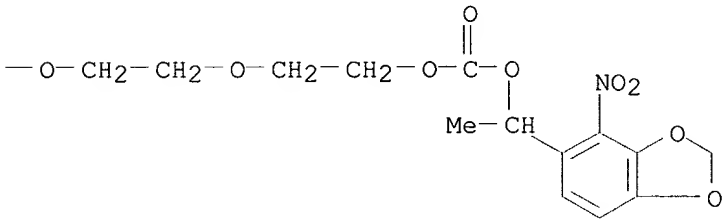


RN 247934-62-9 HCAPLUS
CN 2,5,8,11,14,17,20,22-Octaoxa-21-phosphatetracosanoic acid, 21-[bis(1-methylethyl)amino]-24-cyano-, 1-(4-nitro-1,3-benzodioxol-5-yl)ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



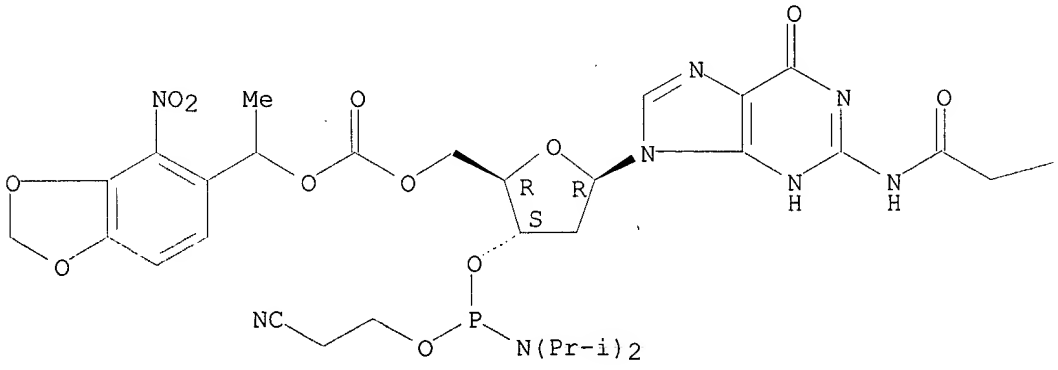
PAGE 1-B



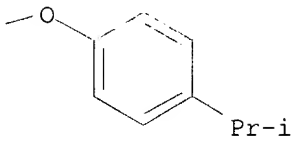
RN 247934-63-0 HCAPLUS
CN Guanosine, 2'-deoxy-N-[[4-(1-methylethyl)phenoxy]acetyl]-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] 5'-[1-(4-nitro-1,3-benzodioxol-5-yl)ethyl carbonate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Affymax Technologies	1995			WO 9511995 A1	HCAPLUS
Drmanac	1989	4	114	GENOMICS	HCAPLUS
Fodor	1995			US 5445934 A	HCAPLUS
Fodor	1996			US 5489678 A	HCAPLUS

L85 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:670078** HCAPLUS
DN **131:282383**
TI Nucleic acid analysis by hybridization to probe arrays
IN Fodor, Stephen P. A.; Lipshutz, Robert J.; Huang, Xiaohua
PA **Affymetrix, Inc., USA**
SO U.S., 29 pp., Cont. of U. S. Ser. No. 505,919.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5968740	A	19991019	US 1997-811829	19970305
	US 6284460	B1	20010904	US 1997-877196	19970617
	US 6268152	B1	20010731	US 2000-543789	20000406
	US 2002177131	A1	20021128	US 2001-776768	20010206
PRAI	US 1995-505919	A1	19950724		
	US 1993-82937	B1	19930625		
	US 1997-877196	A1	19970617		
	US 2000-543789	A1	20000406		

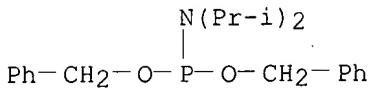
AB The title method comprises exposing a target nucleic acid to an array of probes shorter than the target nucleic acid. To identify whether the target nucleic acid is complementary to a probe in the array, a core probe is identified which has a high affinity for the target and then the **binding** characteristics of all probes with a single base mismatch is compared to that of the core probe. If the single base mismatch probes exhibit a characteristic **binding** or affinity pattern, then the core probe is exactly complementary to at least a portion of the target nucleic acid. The method can be extended to sequence a target nucleic acid by evaluating the **binding** affinity of probes that can be termed "left" and "right" extensions of the probe. The correct left and right extensions of the core are those that exhibit the strongest **binding** affinity and/or a specific hybridization pattern of single base mismatch probes. The process is the repeated to provide addnl. left and right extensions of the core probe and to provide the sequence of the nucleic acid target. In diagnostic applications, a target is expected to have a particular sequence. To det. if the target has the expected

sequence, an array of probes is synthesized that includes a complementary probe and all or some subset of all single base mismatch probes. Through anal. of the hybridization pattern of the target to such probes, it can be detd. if the target has the expected sequence and, if not, the sequence of the target may optionally be detd. A method for **light**-directed synthesis of oligonucleotides and oligonucleotide arrays is also described.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anon	1989			WO 8910977	HCAPLUS
Anon	1989			WO 8911548	HCAPLUS
Anon	1990			WO 0392546	
Anon	1990			WO 9000626	HCAPLUS
Anon	1990			WO 9003382	HCAPLUS
Anon	1992			WO 9210092	HCAPLUS
Anon	1992			WO 9210588	HCAPLUS
Anon	1993			WO 9317126	HCAPLUS
Anon	1988		39	Strategene Catalog	
Chetverin And Kramer	1993	30	215	Biosystems	
Chetverin And Kramer			1	Novel Oligonucleotid	
Chetverin And Kramer			1	Total Genome Sequenc	
Drmanac	1993			US 5202231	HCAPLUS
Elder	1992		1	Maximum Entropy and	
Hagstrom	1992			Argonne Nat'l Lab Pr	
Khrapko	1989	256	118	FEBS Letts	HCAPLUS
Lipshutz	1993	11	637	J Biomolecular Struc	HCAPLUS
Lysov	1988	303	1508	(Translation) Doklad	HCAPLUS
Macevicz	1991			US 5002867	HCAPLUS
Maxam	1977	74	560	Proc Natl Acad Sci U	HCAPLUS
Pirrung	1992			US 5143854	HCAPLUS
Sambrook	1989	11.45		Molecular Cloning	
Sanger	1977	74	5463	Proc Natl Acad Sci U	HCAPLUS
Southern	1992	13	1008	Genomics	HCAPLUS
Stockham	1993			US 5273636	

L85 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:667155 HCAPLUS
DN 130:33604
TI 6-N-(N-methylanthranylamido)-4-oxo-hexanoic acid: a new fluorescent protecting group applicable to a new DNA sequencing method
AU Rasolonjatovo, Isabelle; Sarfati, Simon R.
CS Unite Chimie Organique, ERS 558, Institut Pasteur, Paris, 75724, Fr.
SO Nucleosides & Nucleotides (1998), 17(9-11), 2021-2025
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB 6-Amino-4-oxo-hexanoic acid with a fluorescent probe attached to the amino function, deriv. of the levulinic acid has been developed for protection of hydroxyl groups. It is introduced by reaction of its sym. anhydride and rapidly removed under mild conditions using a hydrazine-pyridinium acetate buffer at near neutral pH and room temp. It can be used within the scope of a new DNA sequencing method and as a sensitive detectable protecting group.
IT **108549-23-1**, Dibenzyl N,N-diisopropylphosphoramidite
RL: RCT (Reactant); RACT (Reactant or reagent)
(6-N-(N-methylanthranylamido)-4-oxo-hexanoic acid: new fluorescent protecting group applicable to new DNA sequencing method)
RN 108549-23-1 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bittman, R	1996	37	391	J Lipid Res	HCAPLUS
Canard, B	1994	148	1	Gene	HCAPLUS
Canard, B	1995	92	10859	Proc Natl Acad Sci U	HCAPLUS
Hoard, D	1965	87	1141	J Am Chem Soc	
Leikauf, E	1995	51	5557	Tetrahedron Lett	HCAPLUS
Moffatt, J	1964	42	599	Can J Chem	HCAPLUS
Moffatt, J	1964	83	649	J Am Chem Soc	
Nakamura, E	1987	109	8056	J Am Chem Soc	HCAPLUS
Rasolonjatovo, I	1997			Nucleosides & Nucleo	
Schaller, G	1963	85	3821	J Am Chem Soc	
Smith, M	1958	80	1141	J Am Chem Soc	HCAPLUS
van Boom, J	1978	97	73	Rec Trav Chim Pays-B	HCAPLUS
van Boom, J	1976	52	4875	Tetrahedron Lett	
Wang, J	1997	38	739	Tetrahedron Lett	HCAPLUS
Yu, K	1988	29	979	Tetrahedron Lett	HCAPLUS

L85 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:383643** HCAPLUS
DN **129:171062**
TI **Light** scattering by metal sol labels on high density DNA probe arrays
AU Trulson, Mark O.; Walton, Ian D.; Suseno, Audrey; Matsuzaki, Hajime; Stern, David
CS **Affymetrix, Santa Clara, CA, 95051, USA**
SO Proceedings of SPIE-The International Society for Optical Engineering (1998), 3259(Systems and Technologies for Clinical Diagnostics and Drug Discovery), 234-240
CODEN: PSISDG; ISSN: 0277-786X
PB SPIE-The International Society for Optical Engineering
DT Journal
LA English
AB We have been exploring the use of **light** scattering as a means to detect the **binding** of nucleic acids to high d. DNA probe arrays. Initial work has concd. on the use of 100 nm gold particles conjugated to monoclonal antibodies. A probe array scanner that utilizes an arc lamp source and a "photocopier grade" linear CCD detector has been developed. The optical configuration of the scanner maximizes dynamic range and minimizes optical backgrounds. Initial development of **light** scattering detection for the p53 cancer gene application shows that functional performance may be obtained that is essentially equiv. to existing fluorescence detection methodol.

L85 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:314610 HCAPLUS
DN 128:291131
TI Reversible covalent binding of nucleic acids to microprojectiles for transformation of cells by microprojectile bombardment
IN Wittig, Burghardt; Junghans, Claas
PA Soft Gene G.m.b.H., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent

LA German
FAN.CNT 2

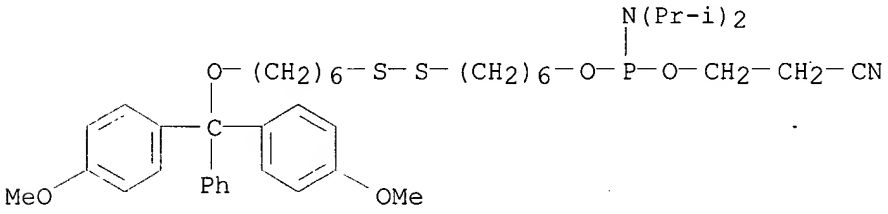
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19648625	A1	19980514	DE 1996-19648625	19961113
	WO 9821322	A1	19980522	WO 1997-DE2704	19971113
	W: AU, BR, CA, CU, CZ, DE, EE, HU, IL, JP, KR, LT, LV, MX, NZ, PL, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9853086	A1	19980603	AU 1998-53086	19971113
	EP 941318	A1	19990915	EP 1997-949949	19971113
	EP 941318	B1	20010117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 198767	E	20010215	AT 1997-949949	19971113
	ES 2155702	T3	20010516	ES 1997-949949	19971113
	US 6451593	B1	20020917	US 1999-310842	19990512
PRAI	DE 1996-19648625	A	19961113		
	WO 1997-DE2704	W	19971113		

AB A method of improving the efficiency of transfer of nucleic acids to their target tissues using microprojectile bombardment by attaching the nucleic acids to the microprojectile through a covalent bond that is readily cleaved in target cells is described. The method further involves covalently closing the ends of linear DNA to protect from exonucleases. Bonding is preferably via a sulfur-gold bond that can be readily cleaved by the thiol compds. present in cells, e.g. glutathione. The use of Thiol modifier C6 S-S to bond DNA to gold particles is demonstrated. Similarly, DNA can be coupled to aluminum oxide using carbodiimides.

IT **148254-21-1D**, reaction products with nucleic acids
RL: RCT (Reactant); RACT (Reactant or reagent)
(reversible bonding of nucleic acids to gold using; reversible covalent binding of nucleic acids to microprojectiles for transformation of cells by microprojectile bombardment)

RN 148254-21-1 HCAPLUS

CN Phosphoramidous acid, bis(1-methylethyl)-, 6-[[6-[bis(4-methoxyphenyl)phenylmethoxy]hexyl]dithio]hexyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)

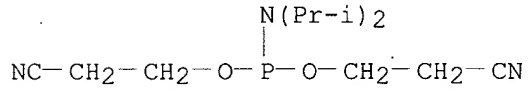


L85 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:708479 HCAPLUS
DN 127:356385
TI Libraries of Multifunctional RNA Conjugates for the Selection of New RNA Catalysts
AU Hausch, Felix; Jaeschke, Andres
CS Institut fuer Biochemie, Freie Universitaet Berlin, Berlin, 14195, Germany
SO Bioconjugate Chemistry (1997), 8(6), 885-890
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB An in vitro selection system was developed for the selection of RNA mols. catalyzing bimol. reactions between small reactants. The system is based on the direct selection protocol and involves libraries of multifunctional

RNA conjugates rather than unmodified RNA transcripts. For the prepn. of RNA conjugate libraries, a dinucleotide analog has been designed and synthesized contg. a poly(ethylene glycol) linker with an embedded photocleavage site and a terminal attachment site for coupling potential reactants. Reactants are first coupled to the dinucleotide analog by activated ester chem. and then ligated to the 3'-ends of enzymically prepd. RNA pool mols., giving libraries of complex conjugates. Species that become attached to biotin on incubation with a biotinylated partner are isolated using streptavidin-derivatized matrixes and then subjected to a photocleavage step. Selective cleavage of the linker releases only those RNA species in which reaction has taken place at the linker-coupled reactant, while products with the biotin attached to internal positions of the RNA part remain immobilized. Efficient photocleavage is achieved by laser irradn. at 355 nm, and the released RNAs are intact and amplifiable by reverse transcription. All steps are shown to be compatible with the overall selection procedure, as was shown by performing a model selection cycle. Besides allowing a broader scope of reaction types to be selected for, the strategy relieves the RNA from the requirement to possess substrate properties as well as catalytic activity, and the use of a cleavable linker will suppress the selection of catalysts for side reactions.

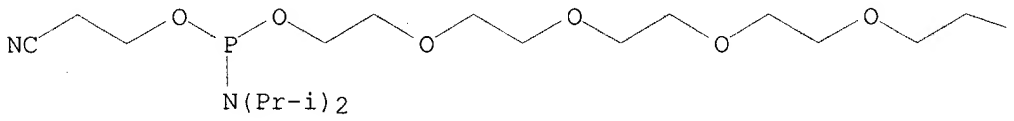
IT **102690-88-0 125607-09-2 168329-40-6 198327-87-6D**, derivs.
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of libraries of multifunctional RNA-linker-reactant for selection of new ribozymes)

RN 102690-88-0 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, bis(2-cyanoethyl) ester (9CI) (CA INDEX NAME)

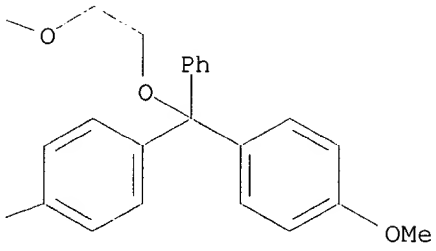


RN 125607-09-2 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-cyanoethyl 19,19-bis(4-methoxyphenyl)-19-phenyl-3,6,9,12,15,18-hexaoxanonadec-1-yl ester (9CI) (CA INDEX NAME)

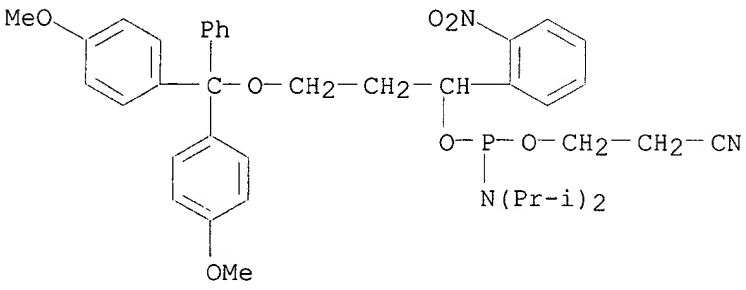
PAGE 1-A



PAGE 1-B

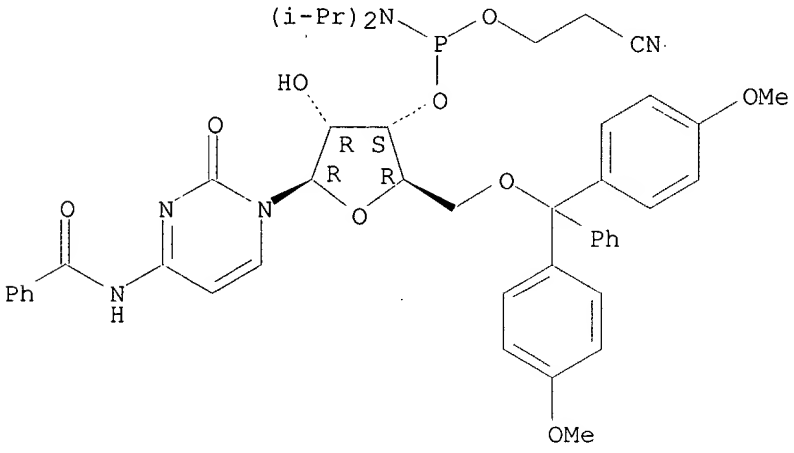


RN 168329-40-6 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 3-[bis(4-methoxyphenyl)phenylmethoxy]-1-(2-nitrophenyl)propyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)



RN 198327-87-6 HCAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

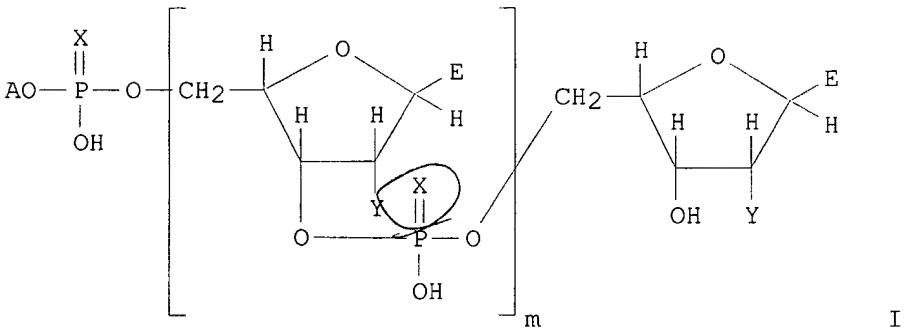


L85 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:293717 HCAPLUS
DN 122:291447
TI Organic super-thin film of oligonucleotide derivative and method for its preparation
IN Debitsudo, Arubaguri
PA Mitsubishi Chem Ind, Japan

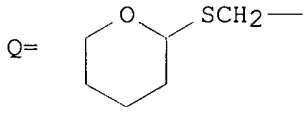
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06039275	A2	19940215	JP 1992-196823	19920723
PRAI	JP 1992-196823		19920723		

OS MARPAT 122:291447
GI



I

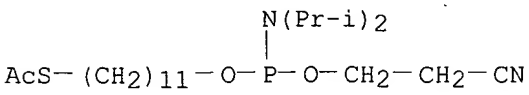


AB An org. super-thin film (Langmuir-Blodgett film) having hydrogen bondings formed between a pair of complimentary nucleic acid bases is formed on a metal surface by bonding the org. thin film through S atom. It comprises a (un)protected SH-contg. oligonucleotide [I; A = RS(CR1R1)n; wherein R = H or HS-protective group and n = integer .gtoreq.8; R1 = H, C1-3 alkyl; E = nucleic acid base; X = S, O; Y = H, OH; m = 1-20] and its complimentary oligonucleotide which are hydrogen-bonded to each other through a pair of complimentary nucleic acid bases. It is formed by dipping a heavy metal plate in a soln. of oligonucleotide I to form a monomol. film of I on the metal surface and then dipping the latter monomol. film in a soln. of the complimentary oligonucleotide of I to form a bimol. film. This org. super-thin film is suitable as materials for various censors and mol. devices. Thus, adenine oligonucleotide thiophosphate I [A = HS(CH2)11, X = S, Y = H, m = 4, E = 9-adenyl] (II) was prepd. by the solid-phase method using a DNA synthesizer. II 0.05 mM and dodecanethiol 0.5 .mu.M were dissolved in EtOH and a Si wafer (1.2 cm .times. 1.2 cm) sequentially vapor-deposited with 250 .ANG. Cr film and 15,000 .ANG. Au film was dipped in the resulting soln. at 25.degree. for 24 h and pulled out to give a monomol. film (19 .ANG.) consisting of a mixt. of II and dodecanethiol. The Si wafer substrate was then dipped in a soln. of thymine oligonucleotide thiophosphate I (A = Q, X = S, Y = H or OH, m = 4, E = thyminyl) in 1.0 M NaCl at 25.degree. for 1 h, pulled out, and washed with EtOH to give a bimol. film (42 .ANG.).

IT **156648-15-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate for prepn. of complimentary oligonucleotides and bimol. films)

RN 156648-15-6 HCAPLUS

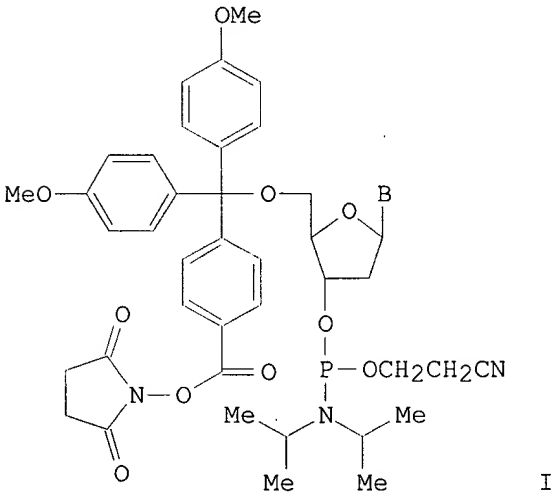
CN Ethanethioic acid, S-[11-[[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]oxy]undecyl] ester (9CI) (CA INDEX NAME)



L85 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1992:37531 HCAPLUS
DN 116:37531
TI Reversible modification of biological compounds for detection, separation and purification thereof
IN Coull, James M.; Gildea, Brian; Koester, Hubert
PA Millipore Corp., USA
SO Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 424819	A1	19910502	EP 1990-120093	19901019
	EP 424819	B1	19941228		
	R: DE, FR, GB, IT, NL, SE				
	US 5410068	A	19950425	US 1989-425740	19891023
	JP 03279371	A2	19911210	JP 1990-283585	19901023
PRAI	US 1989-425740		19891023		

OS MARPAT 116:37531
GI



I

AB Compds. and methods are provided for the reversible modification of natural products, natural product synthons, biopolymers, or biopolymer synthons, e.g. nucleosides, nucleotides, oligonucleosides. The modification allows a variety of chemistries to be performed on these compds., yet can be removed to regenerate functional groups on the natural product, biopolymer, or synthon of interest. The compds. of the invention serve as a protecting group for a functional group on the natural product, biopolymer, or synthon, and as a linking group for attaching a modifying

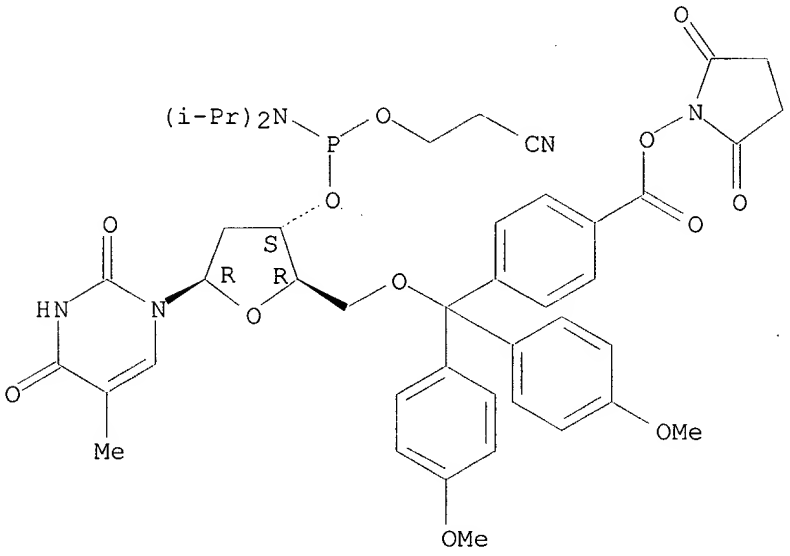
moiety thereto. Prepn. of N-succinimidyl-4-[bis-4-(methoxyphenyl)-5'-O-(3'-O-(N,N-diisopropylamino-2-cyanoethylphosphinyl)-2-deoxynucleosidyl)-methyl] benzoates (I), e.g. I (B = thymine), is described. The modified nucleosides were used in the synthesis of biotin- and fluorescein-labeled polymerase chain reaction (PCR) oligonucleotide primers. Use of the 5'-modified oligonucleotides of the invention for the purifn. of PCR products was demonstrated.

IT **132454-46-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for polymerase chain reaction primer prepn., amplified nucleic acid isolation in relation to)

RN 132454-46-7 HCAPLUS

CN Thymidine, 5'-O-[[4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]phenyl]bis(4-methoxyphenyl)methyl]-, 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L85 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2003 ACS

AN **1990:139562** HCAPLUS

DN **112:139562**

TI Phosphoramidite reagents for functionalizing oligonucleotides with amine,hydroxyl, or thiol groups

IN Levenson, Corey; Chang, Chu An; Oakes, Fred T.

PA Cetus Corp., USA

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

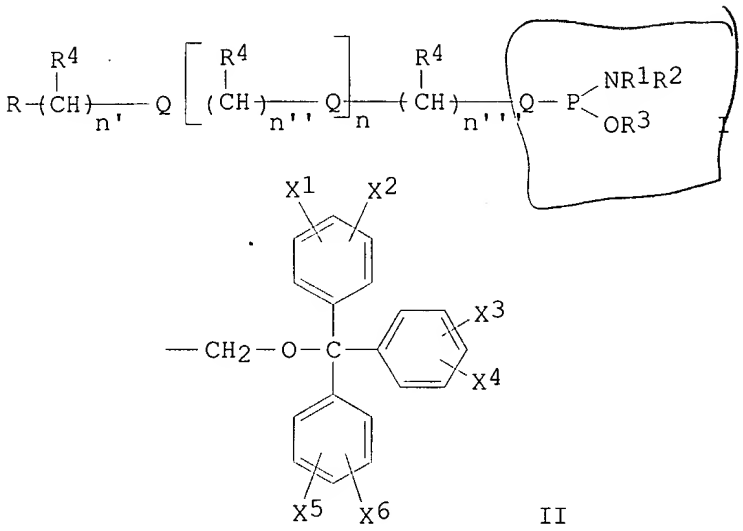
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8902931	A1	19890406	WO 1988-US3212	19880919
	W: DK, FI, JP, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4914210	A	19900403	US 1987-104200	19871002
	EP 380559	A1	19900808	EP 1988-908841	19880919
	EP 380559	B1	19931222		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03501383	T2	19910328	JP 1988-508099	19880919

	AT 98996	E	19940115	AT 1988-908841	19880919
	CA 1310600	A1	19921124	CA 1988-578519	19880927
	IL 87879	A1	19930610	IL 1988-87879	19880929
PRAI	US 1987-104200		19871002		
	EP 1988-908841		19880919		
	WO 1988-US3212		19880919		

OS MARPAT 112:139562

GI



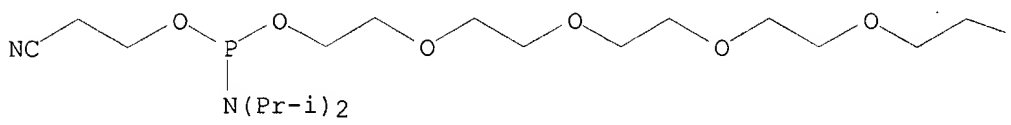
AB Phosphoramidite reagents [I; R1, R2 = H, lower alkyl; R3 = .beta.-cyanoethyl, methyl; R = protected or unprotected amino, sulfhydryl, or hydroxyl moiety; R4 = H, CH2OH or II (X1-X6 = H, lower alkyl, lower alkoxy); Q = O, NH, etc.; n, n', n'', n''' are integers] have a hydrophilic spacer arm and are suitable for introducing functional groups onto oligonucleotides. The reagents are more convenient to use than those of the prior art. Their synthesis and uses are described. An oligonucleotide was coupled with a tritylthio polyether phosphoramidite under std. phosphoramidite coupling procedures to yield a tritylthio oligomer. After detritylation of the oligomer it was incubated with N-maleimido-6-aminocaproyl 4-hydroxy-3-nitrobenzene sulfonate-derivatized horseradish peroxidase at 4 .degree.C for 2 days. Unreacted starting materials were sepd. from the end-products by chromatog. The conjugate was detectable by coincidence of peaks of absorbance at 260 nm and 402 nm (heme group of peroxidase).

IT **125607-09-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for manuf. of oligonucleotide derivs.)

RN 125607-09-2 HCAPLUS

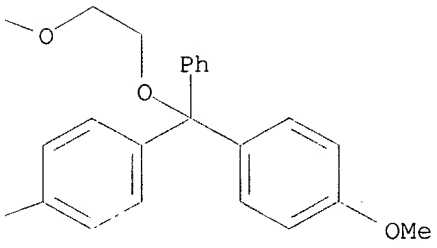
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-cyanoethyl 19,19-bis(4-methoxyphenyl)-19-phenyl-3,6,9,12,15,18-hexaoxanonadec-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

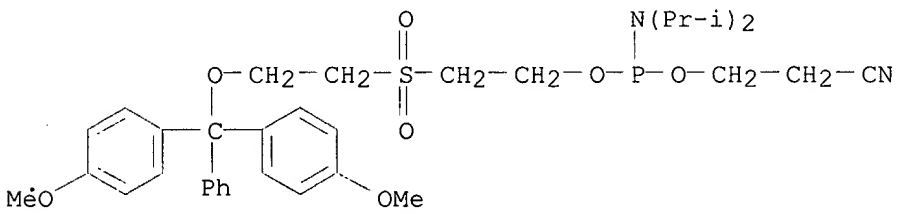


MeO

PAGE 1-B

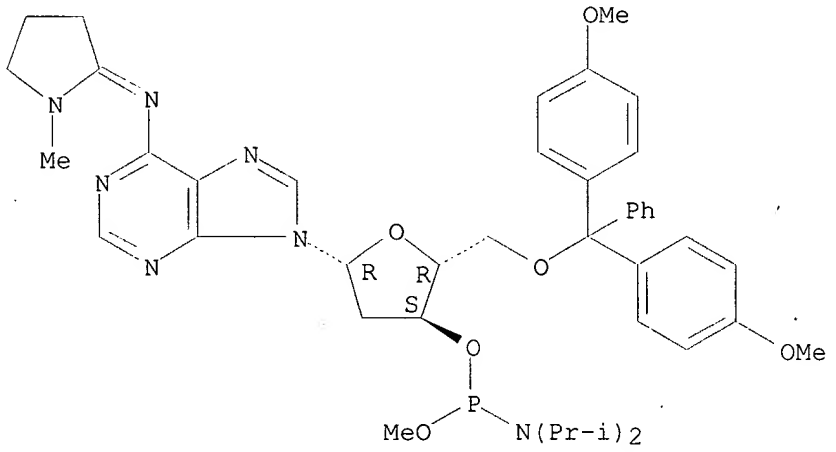


L85 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN **1987:423651** HCAPLUS
DN **107:23651**
TI A chemical 5'-phosphorylation of oligodeoxyribonucleotides that can be monitored by trityl cation release
AU Horn, Thomas; Urdea, Mickey S.
CS Chiron Res. Lab., Chiron Corp., Emeryville, CA, 94608, USA
SO Tetrahedron Letters (1986), 27(39), 4705-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 107:23651
AB A new phosphoramidite-derived reagent, (Me2CH)2NP(OCH2CH2CN)(OCH2CH2SO2CH2 CH2ODMT)(DMT = 4,4'-dimethoxytrityl), for the 5'-phosphorylation of oligodeoxyribonucleotides was developed. Phosphorylation efficiency was detd. by the release of 4,4'-dimethoxytrityl cation in acid.
IT **108783-02-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, reagent for 5'-phosphorylation of oligodeoxyribonucleotides)
RN 108783-02-4 HCAPLUS
CN Phosphoramidous acid, bis(1-methylethyl)-, 2-[[2-[bis(4-methoxyphenyl)phenylmethoxy]ethyl]sulfonyl]ethyl 2-cyanoethyl ester (9CI) (CA INDEX NAME)



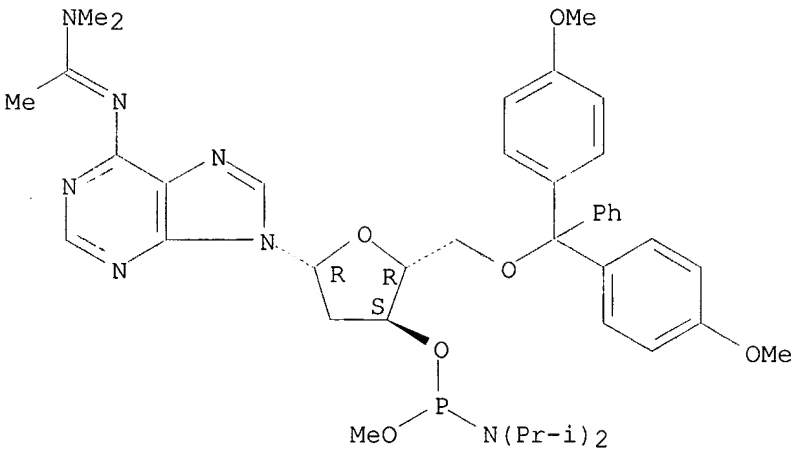
L85 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2003 ACS
AN 1985:560799 HCAPLUS
DN 103:160799
TI Synthesis of oligodeoxynucleotides using the phosphoramidite method
AU Caruthers, M. H.; Barone, A. D.; Bracco, L. P.; Dodds, D. R.; Eisenbeis, S. J.; McBride, L. J.; Nasoff, M. S.; Noble, S. A.; Tang, J. Y.
CS Dep. Chem., Univ. Colorado, Boulder, CO, 80309, USA
SO Studies in Organic Chemistry (Amsterdam) (1985), 20(Nat. Prod. Chem.), 213-25
CODEN: SOCHDQ; ISSN: 0165-3253
DT Journal
LA English
AB An in situ method is described for synthesizing DNA which incorporates a new series of amidine protected deoxynucleosides and bis-dialkylaminophosphines as phosphitylating agents. These procedures were used to generate deoxyoligonucleotides for studying the interaction of cro protein with cro operator. The results of these studies support the current hypothesis on the mechanism of cro protein-cro operator interactions.
IT **88010-87-1P 98532-93-5P 98532-94-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, intermediate in synthesis of oligodeoxynucleotides)
RN 88010-87-1 HCAPLUS
CN Adenosine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-(1-methyl-2-pyrrolidinylidene)-, 3'-[methyl bis(1-methylethyl)phosphoramidite] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



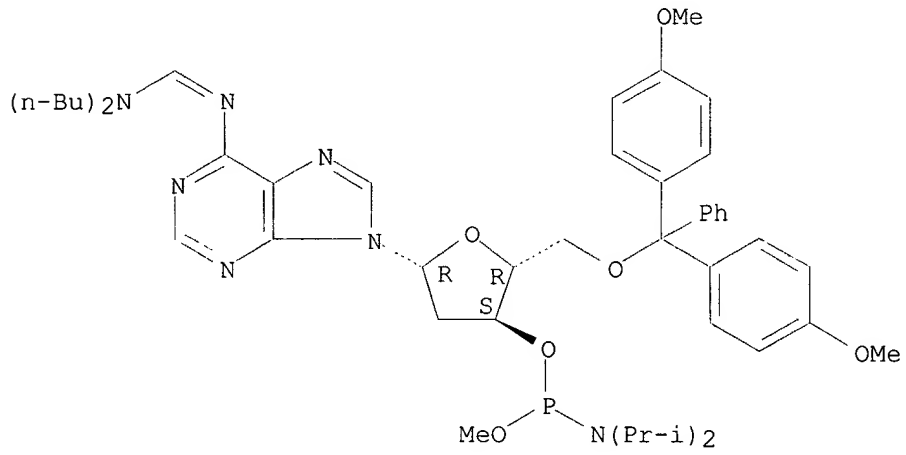
RN 98532-93-5 HCAPLUS
CN Adenosine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-[1-(dimethylamino)ethylidene]-, 3'-(methyl bis(1-methylethyl)phosphoramidite) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 98532-94-6 HCAPLUS
CN Adenosine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-N-[(dibutylamino)methylene]-, 3'-(methyl bis(1-methylethyl)phosphoramidite) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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FILE LAST UPDATED: 13 JAN 2003 <20030113/UP>
MOST RECENT DERWENT UPDATE: 200303 <200303/DW>
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http://www.derwent.com/userguides/dwpi_guide.html <<<

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L98 ANSWER 1 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2002-444944 [48] WPIX
DNC C2002-126774
TI Preparing normalized and/or subtracted cDNAs, comprises preparing uncloned cDNAs and polynucleotides, conducting normalization and/or subtraction, removing tester/driver hybrids and non-hybridized polynucleotide drivers.
DC B04 D16
IN HAYASHIZAKI, Y; HAYASHIZAKI, J
PA (HAYA-I) HAYASHIZAKI Y; (RIKE) RIKEN KK; (RIKA) RIKAGAKU KENKYUSHO
CYC 29
PI CA 2356123 A1 20020225 (200248)* EN 63p C12N015-10
EP 1197552 A2 20020417 (200248) EN C12N015-10
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2002106666 A1 20020808 (200254) C12Q001-68 <--
JP 2002253237 A 20020910 (200274) 25p C12N015-09 <--
ADT CA 2356123 A1 CA 2001-2356123 20010822; EP 1197552 A2 EP 2001-120108 20010822; US 2002106666 A1 US 2001-935592 20010824; JP 2002253237 A JP 2001-256576 20010827
PRAI JP 2000-255402 20000825
IC ICM **C12N015-09**; C12N015-10; **C12Q001-68**
ICS C07H021-04; C12N015-64; **C12P019-34**
AB CA 2356123 A UPAB: 20020730
NOVELTY - Preparing (M1) normalized and/or subtracted cDNAs, comprises preparing uncloned cDNAs (testers) and polynucleotides (drivers) for normalization and/or subtraction, conducting normalization and/or subtraction and removing tester/driver hybrids and non-hybridized polynucleotide drivers, and recovering the normalized and/or subtracted cDNA.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a single or double stranded cDNA or cDNA library obtainable by (M1).

USE - M1 is useful for preparing normalized and/or subtracted nucleic acids, and for preparing one, two or more cDNA libraries. RNA **non-specifically bound** to DNA can be removed, and single stranded cDNA can be isolated (all claimed).

ADVANTAGE - The method maintains a high proportion of long, full coding/length cDNAs in the subtracted/normalized library. Furthermore, the method increases the discovery of new genes relating to results obtained by using standard, full length cDNA libraries prepared based on prior art. The normalized and/or subtracted is an uncloned cDNA, hence the prior art problem of cloning bias against large cDNAs in plasmid libraries and the problem in libraries generated by normalization techniques based on PCR and solid matrices can be avoided, and the advantage of increased discovery of new genes is afforded. The method permits high efficiency removal of mRNA drivers, no relevant cDNA size reduction following hybridization that would affect the frequency of long, full coding/length cDNAs, suitably to both normalization and subtraction, less cross-reactivity between similar but unidentical sequences, and high level performance, reproducibility and ease of handling in terms of both the size of the drivers prepared and the number of libraries.

Dwg.0/5
FS CPI

FA AB; DCN
MC CPI: B04-E01; B04-G01; B04-L05A; B11-C07; B11-C08; B12-K04E; D05-H12; D05-H13; D05-H18
TECH UPTX: 20020730
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The cDNA tester is a single strand reverse transcript of mRNA in the form of uncloned cDNA. Normalization is conducted first, followed by subtraction, or vice versa. The tester and normalization and subtraction drivers are mixed together, and normalization and subtraction are conducted as a single step. The normalized and/or subtracted cDNA is long-strand, full-coding and/or full-length cDNA. M1 further involves adding an enzyme capable of cleaving single strand RNA driver **non-specifically bound** to single strand cDNA, and the cleaved single strand RNA driver is removed. The enzyme is single-strand-specific RNA endonuclease e.g. RNase I, RNase A, RNase 4, RNase T1, RNase T2, RNase 2 or RNase 3, or their mixtures. The cDNA tester is prepared by CAP-trapping the 5' end of RNA. The method involves synthesizing first strand cDNA by means of reverse transcriptase forming mRNA/cDNA hybrids, chemically **binding** a tag molecule to the diol structure of the 5' CAP (7MeGpppN) site of mRNA forming hybrids, trapping long-strand, full-coding, and/or full-length cDNA hybrids, and removing single strand mRNA through digestion with an enzyme capable of cleaving single strand mRNA. The tag molecule is digoxigenin, biotin, avidin or streptavidin. The normalization driver comprises cellular mRNA or single strand cDNA from the same library, the same tissue or the same cDNA population as what is to be normalized. The subtraction driver comprises cellular mRNA or single strand cDNA from a library, tissue or cDNA population differing from what is to be subtracted. The method further involves preparing a second strand of recovering cDNA and performing cloning. The tester/driver hybrid is removed through the use of a matrix comprised of magnetic beads or agarose beads. The magnetic beads or agarose beads are covered by or **bound** to any tag molecule capable of **binding** to tag molecules **bound** to a tester/driver hybrids. The tag molecule is capable of **binding** to avidin, streptavidin, biotin, digoxigenin, antibody or antigen **bound** to a tester/driver hybrid. The antibody covering the beads is an anti-antigen antibody, antibiotin antibody, anti-avidin antibody, anti-streptavidin antibody or anti-digoxigenin antibody. The tester/driver hybrid is removed through the use of streptavidin/phenol. The hydroxy apatite and non-labeled RNA are employed to remove tester/driver hybrid.
RNA **non-specifically bound** to DNA can be removed by processing **non-specifically bound** RNA/DNA hybrids with an enzyme capable of degrading single strand RNA. Single stranded DNA can be isolated by treating a hybrid comprising RNA **non-specifically bound** to cDNA with an enzyme capable of degrading single strand RNA, removing the degraded single strand RNA, and recovering the cDNA.

ABEX
EXAMPLE - A cDNA sample, 5 microl of 0X TdT buffer, 5 microl of 50 microM dGTP, 5 microl of 10 mM CoCl2, and 4o U terminal deoxynucleotidyl transferase were admixed and incubated at 37degreesC for 30 minutes. The cDNA was treated with proteinase K and precipitated. After the tail length had been checked, the cDNA was employed as cDNA tester in normalization and/or subtraction. mRNA drivers comprised aliquots of starting mRNA. The subtractive drivers consisted of bulk run-off transcripts prepared from cloned mini libraries and rearrayed libraries prepared from the non-redundant RIKEN cDNA encyclopedia using T7 and T3 RNA. The RNA drivers and cDNA were deproteinated and precipitated. Oligo-dG-tailed cDNA was used as a substrate, which was mixed with RNA drivers and blocking oligonucleotides (biotin-dG5 to -dG30) to hybridize to the C-stretch present in the subtracting driver and with oligo-dT primer to block the polyA sequences. Hybridization was typically carried out at RoT values of 1-500 in a buffer containing 80% formamide, 250 mM Sodium chloride, 25 mM

HEPES (pH 7.5), and 5 mM EDTA (ethylene diamine tertraacetate). Hybridization was carried out at 42degreesC in a dry oven. After hybridization, the sample was precipitated and incubated for 30 minutes on ice. The sample was then centrifuged and washed. The tester/driver hybrids obtained were treated with RNase I to remove the mRNA normalization and subtraction drivers bound **non-specifically** to the tester cDNA. Separately, 50 microl of MPG-streptavidin magnetic beads were prepared for each microg of biotinylated driver RNA. To each 50 microl of beads, 10 microg of tRNA was added as a blocking reagent and the beads were incubated at room temperature for 10-20 minutes. The blocked beads were mixed with the redissolved tester/driver mixture and the entire sample was incubated at room temperature for 15 minutes with occasional gentle mixing. After removing the beads, the supernatant containing the single-strand normalize/subtracted cDNA, was recovered. The radioactivity of the labeled samples was measured before and after the procedure in order to estimate the yield of normalization/subtraction.

L98 ANSWER 2 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2002-428569 [46] WPIX
DNC C2002-121716
TI In vitro amplification of a nucleic acid sequence using a primer based amplification reaction and oligonucleotide primers containing particular modifications.
DC B04 D16
IN LAIRD, W J; NIEMIEC, J T
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE DIAGNOSTICS GMBH
CYC 28
PI EP 1201768 A2 20020502 (200246)* EN 22p C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
CA 2359838 A1 20020425 (200246) EN C12N015-10
JP 2002291490 A 20021008 (200281) 21p C12N015-09 <--
ADT EP 1201768 A2 EP 2001-125022 20011020; CA 2359838 A1 CA 2001-2359838 20011024; JP 2002291490 A JP 2001-326463 20011024
PRAI US 2000-243182P 20001025
IC ICM **C12N015-09**; C12N015-10; **C12Q001-68**
ICS **C12P019-34**
AB EP 1201768 A UPAB: 20020722
NOVELTY - A kit (I) for carrying out a nucleic acid amplification reaction where the kit comprises a pair of primers where one primer contains a modified nucleotide within the three 3' terminal nucleotide positions and the modified nucleotide is selected from (A) consisting of 2'-O-methyl nucleotides, 2'-fluoro-nucleotides, 2'-amino nucleotides and arabinose nucleotides.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for amplifying (M1) a nucleic acid target sequence where the method comprises carrying out a primer-based amplification reaction in a reaction mixture comprising a pair or primers as in (I).

USE - (I) is useful for performing amplification whilst preventing **non-specific** amplification.

ADVANTAGE - The modified primers of the invention reduce **non-specific** amplification by increasing the time required for the initial primer extension to occur which reduces the likelihood that an unstable transient hybridization duplex is formed.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-E01; B04-E05; B11-C08E3; B11-C08E5; D05-H12D1; D05-H18B
TECH UPTX: 20020722
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Kit: The modified nucleotide is at the 3' terminal position. Each primer of the pair of primers independently contains a modified nucleotide within the three 3' terminal nucleotide positions where each modified nucleotide is selected from group

(A).

ABEX

EXAMPLE - Amplifications were carried out using 3'-terminal 2'-O-modified primers. The primer dimer C-T values obtained were compared to those obtained in reactions using unmodified primers in which C-T values of 37-38 were observed. (C-T values refer to the exact number of cycles required to reach the arbitary fluorescence level (AFL). The data demonstrated that the use of at least one primer that incorporated a 3' terminal 2'-O-Me nucleotide delays the formation of primer dimer in template-free reactions. In particular in almost all reactions a C-T greater than 40 was obtained.

L98 ANSWER 3 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2001-246729 [26] WPIX
DNC C2001-074354
TI Reversibly inactivating thermostable DNA polymerase or ligase for use in a PCR reaction or kit comprises mixing dried enzyme with anhydrous dicarboxylic acid in an anhydrous aprotic solvent.
DC B04 D16
IN LOUWRIER, A
PA (ADBI-N) ADVANCED BIOTECHNOLOGIES LTD
CYC 27
PI EP 1078984 A1 20010228 (200126)* EN 10p C12N009-99
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
GB 2353530 A 20010228 (200126) C12N009-99
GB 2353530 B 20010627 (200137) C12N009-99
JP 2002199877 A 20020716 (200261)# 7p C12N009-12
US 6479264 B1 20021112 (200278) C12N009-00
ADT EP 1078984 A1 EP 2000-307337 20000825; GB 2353530 A GB 2000-21086 20000825; GB 2353530 B GB 2000-21086 20000825; JP 2002199877 A JP 2000-364771 20001130; US 6479264 B1 US 2000-649707 20000825
PRAI GB 1999-20194 19990827; JP 2000-364771 20001130
IC ICM C12N009-00; C12N009-12; C12N009-99
ICS C08H001-00; **C12N015-09**; **C12P019-34**; C12Q001-48; **C12Q001-68**

AB EP 1078984 A UPAB: 20010515
NOVELTY - Reversibly inactivating thermostable DNA polymerase or ligase comprising mixing dried enzyme with anhydrous dicarboxylic acid in an anhydrous aprotic solvent, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a reversibly inactivated DNA polymerase or ligase produced by the method; and

(2) a PCR kit comprising the reversibly inactivated DNA polymerase.

USE - The method produces a reversibly inactivated thermostable DNA polymerase or ligase (claimed). The polymerase can be incorporated into a PCR kit (claimed).

ADVANTAGE - The reversibly denatured polymerase can be heat reactivated prior to a PCR reaction and thus overcomes the problem of **non-specific** primer annealing and extension. The method excludes water and therefore does not suffer from pH based denaturation of the enzyme and is more rapid (5 hours rather than 12 hours) than prior art methods.

Dwg.0/4

FS CPI
FA AB; DCN
MC CPI: B04-E01; B04-E05; B04-L04A; B04-L08; B11-C08E3; B11-C08E5; B11-C09; B12-K04; B12-K04F; D05-H18B; D05-H19B
TECH UPTX: 20010515
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method : The dried polymerase or ligase (less than 5-10% in the presence of lyoprotectants) is first suspended in the aprotic organic solvent and the anhydrous dicarboxylic

acid (e.g. citraconic anhydride or cis-aconitic anhydride) is added subsequently. The reaction takes place at a temperature greater than 30 degreesC. The solid phase comprising the inactivated enzyme is then recovered and washed with an organic solvent (e.g. hexane) before being dried.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Solvent: The aprotic solvents are t-methyl butyl ether (t-MBE), butyl ether, carbon tetrachloride, cyclohexanone, ethyl acetate, methyl ethyl ketone, methyl pentanone, propyl ether, pyridine and sulfolane.

ABEX

EXAMPLE - 50000 units of DNA polymerase from Thermus aquaticus was vacuum dried in 2% sucrose as lyoprotectant in double-distilled, de-ionized water. The dried enzyme was then added to 5 ml anhydrous t-methyl butyl ether (t-MBE), 5% v/v, and an excess of citraconic anhydride added to modify the lysine groups. The reaction was incubated at 37 degreesC for 5 hours after which the powder was washed 4 times with 10 ml hexane. The enzyme was stored at -20 degreesC either as a powder or in storage buffer (20 mM Tris-HCl, 100 mM potassium chloride, 0.1 mM ethylenediamine-tetraacetic acid, 1 mM dithiothreitol, 0.5% (v/v) Tween 20, 0.5% Nonidet P40, 50% glycerol, pH 9.2) at a concentration of 5 units/mul.
The enzyme was then reactivated by incubation at 95 degreesC for 15 minutes prior to performing PCR on human DNA using beta-actin primers:
(i) 5' ATTTGCGGTGGACGATGGAG 3'
(ii) 5' AGAGATGGCCACGGCTGCTT 3'
The reactivated enzyme produced the desired product whereas a control with no activation step produced no product.

L98 ANSWER 4 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-516095 [47] WPIX
DNC C2000-154056
TI Reducing primer-dimer formation during target nucleic acid amplification involves contacting primer-carrier admixture comprising amplification primers and carrier nucleic acid with target nucleic acid.
DC B04 D16
IN BACKUS, J W; PRESTON, G M
PA (ORTH) ORTHO CLINICAL DIAGNOSTICS INC; (ORTH) ORTHO CLINICAL DIAGNOSTICS CORP; (JOHJ) JOHNSON & JOHNSON CLINICAL DIAGNOSTICS
CYC 32
PI EP 1026261 A2 20000809 (200047)* EN 12p C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 2000014877 A 20000810 (200047) C12Q001-68 <--
NO 2000000538 A 20000804 (200050) C12Q001-68 <--
CA 2295942 A1 20000803 (200052) EN C12N015-10
JP 2000279184 A 20001010 (200056) 29p C12N015-09 <--
CN 1271019 A 20001025 (200104) C12Q001-68 <--
KR 2000076606 A 20001226 (200134) C12Q001-68 <--
US 6300075 B1 20011009 (200162) C12Q001-68 <--
ADT EP 1026261 A2 EP 2000-300790 20000201; AU 2000014877 A AU 2000-14877 20000202; NO 2000000538 A NO 2000-538 20000202; CA 2295942 A1 CA 2000-2295942 20000201; JP 2000279184 A JP 2000-32660 20000203; CN 1271019 A CN 2000-104638 20000203; KR 2000076606 A KR 2000-5497 20000203; US 6300075 B1 Provisional US 1999-118495P 19990203, US 2000-493351 20000128
PRAI US 1999-118495P 19990203; US 2000-493351 20000128
IC ICM **C12N015-09**; C12N015-10; **C12Q001-68**
ICS **C12P019-34**; C12Q001-48
AB EP 1026261 A UPAB: 20000925
NOVELTY - Reducing (R) the formation of primer-dimer or amplification of **non-specific** nucleic acids (NA) for specific amplification of a target NA (I) involves preparing a primer/carrier admixture (PCA) comprising one or more oligonucleotide amplification primers (II) and carrier NA and contacting PCA with (I), one or more

magnesium salts and NA polymerase.
USE - Useful in diagnostic tests for infectious microorganisms.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-E01; B04-E05; B04-G03; B04-L04A; B11-C08E5; B12-K04A4; B12-K04F; D05-H04; D05-H05; D05-H07; D05-H11; D05-H12A; D05-H12D1; D05-H18B
TECH UPTX: 20000925
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (R), the carrier NA is DNA, RNA or peptide nucleic acid (PNA). The DNA is calf thymus DNA. The carrier NA is present in the amplification reaction at the concentration of 1-100 (preferably 5-75 microg/ml), and the admixture is maintained at the temperature less than about 90 - 100degreesC, prior to initiation of amplification reaction and prior to initiating thermal cycling. The polymerase comprises Taq polymerase and magnesium salts comprises magnesium chloride. The admixture further comprises anti-polymerase antibody, an exonuclease, a glycosylase or their combinations.
ABEX
EXAMPLE - A master mix was formulated which contained eleven primers such as;
5'-CGCCAGCGTGGACCATCAAGTAGTAA-3', 5'-CACGATCCTGGAGCAGACACTGAAGA-3', Tris buffer, dNTPs, AmpliTaq, and two AmpliTaq triggering antibodies. Master mixes were prepared without and with calf thymus DNA (group I and group II, respectively). To 50 microl aliquots of the master mixes 16 mM of magnesium chloride and 25 microl of target mix (containing 13.3 copies of Internal positive control target nucleic acid (NA) in 20 microl of sodium hydroxide) were added. In one set of reaction mixtures, the IPC primers were non-thiolated while in a second set, the IPC primers were thiolated. All reactions were performed in duplicate. 75 microl aliquots of the mixtures were added to blank NA pouches. After amplification by PCR, the products were removed from the pouches and resolved by electrophoresis and amplified DNA product was detected using ethidium bromide staining. The group II amplification reactions produced stronger specific product bands and weaker **non-specific** product bands compared with group I.

L98 ANSWER 5 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-328943 [28] WPIX
DNC C2000-099675
TI Novel method of stabilizing duplex formation, or destabilizing **non-specific** duplex formation using primer containing modified nucleotide analogs, useful for preventing mispriming during PCR, RACE, DNA synthesis or sequencing.
DC B04 D16
IN DAS, M; PELLETIER, J
PA (UYMC-N) UNIV MCGILL
CYC 90
PI WO 2000020630 A1 20000413 (200028)* EN 45p C12Q001-68 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 9960732 A 20000426 (200036) C12Q001-68 <--
CA 2246623 A1 20000407 (200036) EN C12N015-10
EP 1117826 A1 20010725 (200143) EN C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002532063 W 20021002 (200279) 48p C12N015-09 <--
ADT WO 2000020630 A1 WO 1999-CA933 19991006; AU 9960732 A AU 1999-60732 19991006; CA 2246623 A1 CA 1998-2246623 19981007; EP 1117826 A1 EP

1999-947148 19991006, WO 1999-CA933 19991006; JP 2002532063 W WO 1999-CA933 19991006, JP 2000-574722 19991006

FDT AU 9960732 A Based on WO 200020630; EP 1117826 A1 Based on WO 200020630; JP 2002532063 W Based on WO 200020630

PRAI CA 1998-2246623 19981007

IC ICM **C12N015-09**; C12N015-10; **C12Q001-68**
ICS **C12P019-34**

AB WO 200020630 A UPAB: 20000613

NOVELTY - Stabilizing duplex formation, or destabilizing **non-specific** duplex formation, between an oligonucleotide and a target nucleic acid (NA), comprises incubating the target NA with a modified oligonucleotide (I) comprising a homopolymeric sequence having a modification which decreases or abrogates H-bonding between the oligonucleotide and the target NA, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) increasing the proportion of full length cDNA clones in a library using a modified oligo d(T) as in (I) during first strand synthesis of a modified oligonucleotide as in (I) during second strand synthesis;

(2) a kit for the synthesis of cDNA comprising a modified oligo d(T) primer as in (I);

(3) reducing misprinting events during DNA synthesis, 5' or 3' RACE, or sequencing comprising using a modified oligonucleotide as in (I) to prime DNA synthesis, 5' or 3' RACE, or sequencing;

(4) a kit for the 5' RACE comprising a modified oligonucleotide primer as in (I); and

(5) generating bona fide genetic markers using a modified oligonucleotide as in (I) to prime homopolymeric stretches.

USE - The modified oligonucleotide is used to improve discrimination between the targeted homopolymeric sequence and a non-homopolymeric target sequence. It is used to increase the proportion of full length cDNA clones for a library, to reduce mispriming during sequencing, 5' or 3' RACE (rapid amplification of cDNA ends) or DNA synthesis or to generate bona fide genetic markers (all claimed).

The use of an oligo d(T) primer incorporating two 3-nitropyrrole nucleotides on a cDNA clone for eIF-4GII (an eukaryotic translation factor) whose sequence contains an internal A-rich sequence resulted in greater than 95% of products being full length as compared to greater than 95% of products being less than full length when primed with oligo d(T) primers.

DESCRIPTION OF DRAWING(S) - The diagram shows an example of the steps involved in generating cDNA libraries from mRNA.

Dwg.1/6

FS CPI

FA AB; GI; DCN

MC CPI: B04-B03C; B04-E02; D05-H09; D05-H12D1; D05-H18A; D05-H18B

TECH UPTX: 20000613

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The modification is at least 1 universal nucleotide, especially 3-nitropyrrole, incorporated into the homopolymeric sequence. The homopolymer may also incorporate a nucleotide analogue, especially inosine, possibly in a poly d(T) oligonucleotide. The modification may further comprise a phosphate or ribose modification.

ABEX

WIDER DISCLOSURE - The disclosure also relates to primers containing modified nucleosides.

EXAMPLE - An oligonucleotide (designated oligo d(T).I) was synthesized and reverse transcription reactions were performed on in vitro generated eIF-4G mRNA templates with Superscript II. Oligonucleotide primers that were used to prime the first strand synthesis with 0.1 micro g of with oligo d(T).Z (an oligonucleotide where 2 of the nucleotides are replaced by 3-nitropyrrole analogs) or oligo d(T).I. Following the generation of

cDNA products, the mixture was extracted and precipitated by standard methods followed by resuspension in distilled water. An aliquot of the cDNA was loaded onto a 1.2 % alkaline agarose gel and electrophoresis performed at 78 volts for 6.5 hours. The results show that when primed with oligo d(T)15, the major cDNA product is shorter than full length and arises due to mispriming at an internal A-rich site. When primed with oligo d(T).Z, the modified primer is able to correct the mispriming phenomenon and this resulted in over 50% of the cDNA being correctly primed at the poly(A) tail of the mRNA.
5' TTTTTTTIasteriskTTTTTTTTTIasteriskTTTTT 3' (oligo d(T).I)
Where:
Iasterisk = 2'deoxyinosine.

L98 ANSWER 6 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-224719 [19] WPIX
DNC C2000-068780
TI Array for determining linkage of polymorphic forms in target nucleic acid and monitoring expression of mRNA population comprises support having three discrete regions, each containing pool of polynucleotide probes.
DC B04 D16
IN CHEE, M; GENTALEN, E
PA (AFFY-N) AFFYMETRIX INC; (CHEE-I) CHEE M; (GENT-I) GENTALEN E
CYC 89
PI WO 2000011223 A1 20000302 (200019)* EN 53p C12Q001-68 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9955778 A 20000314 (200031) C12Q001-68 <--
EP 1108062 A1 20010620 (200135) EN C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6306643 B1 20011023 (200165) C12M001-34
US 2002106663 A1 20020808 (200254) C12Q001-68 <--
JP 2002523064 W 20020730 (200264) 53p C12N015-09 <--
ADT WO 2000011223 A1 WO 1999-US19069 19990819; AU 9955778 A AU 1999-55778 19990819; EP 1108062 A1 EP 1999-942387 19990819, WO 1999-US19069 19990819; US 6306643 B1 US 1998-138958 19980824; US 2002106663 A1 Cont of US 1998-138958 19980824, US 2001-930536 20010814; JP 2002523064 W WO 1999-US19069 19990819, JP 2000-566474 19990819
FDT AU 9955778 A Based on WO 200011223; EP 1108062 A1 Based on WO 200011223; JP 2002523064 W Based on WO 200011223
PRAI US 1998-138958 19980824; US 2001-930536 20010814
IC ICM C12M001-34; **C12N015-09**; **C12Q001-68**
ICS C07H021-00; C07H021-04; C07H021-09; C12M001-00; **C12P019-34**; G01N033-53; G01N033-566; G01N037-00
AB WO 200011223 A UPAB: 20021105
NOVELTY - An array (A) comprising a support having three discrete regions, each containing a pool of polynucleotide probe(s), where the first region (R1) contains a probe (I), the second region (R2) contains a second probe (II) and the third region (R3) contains (I) and (II), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an array (B) comprising a support having R1-R3, where:
(a) R3 comprises (I) and (II) at a (I):(II) molar ratio (M1);
(b) R1 comprises (I) without (II) or with (II) present at a (I):(II) molar ratio (M2) greater than M1;
(c) R2 comprising (II) without (I) or (I) present at a (I):(II) molar ration (M3) less than M1;
(2) a method of determining linkage of polymorphic forms in a target nucleic acid comprising:

(a) hybridizing a diploid target nucleic acid having first and second polymorphic sites to (A); and

(b) determining a ratio of **binding** of the target nucleic acid to R3 and to R1 and R2 combined to indicate whether the polymorphic form of the first polymorphic site and the polymorphic form of the second polymorphic site are present in the same molecule of the diploid target nucleic acid;

(3) a method of sequencing a target nucleic acid comprising:

(a) hybridizing the target nucleic acid to (A) where (I) is complementary to a known marker;

(b) determining a sequence of a segment of the target nucleic acid from the relative **binding** of the target nucleic acid to the pools of probes; and

(c) mapping the position of the segment in the target sequence relative to the known marker;

(4) a method of monitoring expression of a mRNA population comprising:

(a) providing a sample comprising a population of mRNA molecules;

(b) hybridizing the population of mRNA molecules to (A) where (I) and (II) are complementary to nonoverlapping segments of a known mRNA molecule; and

(c) determining which discrete regions show specific **binding** to the population indicating which of the known mRNA molecules are present; and

(5) a method of analyzing a target nucleic acid:

(a) hybridizing a target nucleic acid to (A); and

(b) comparing **binding** of the target nucleic acid to R3 with the aggregate of the target nucleic acid **binding** to R1 and R2 to determine whether the target nucleic acid includes segments complementary to (I) and (II).

USE - The array and methods are useful for determining linkage of polymorphic forms in a target nucleic acid, sequencing a target nucleic acid, monitoring expression of a mRNA population or analyzing a target nucleic acid.

ADVANTAGE - Using pools of polynucleotide probes reduces the number of array cells required to analyze a given target sequence.

Dwg.0/7

FS CPI

FA AB; DCN

MC CPI: B04-E05; B11-C08E4; B11-C08E5; B11-C09; B12-K04E; B12-K04F; D05-H09; D05-H10; D05-H12D1; D05-H18A

TECH UPTX: 20000419

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Array: (I) and (II) are preferably, respectively, complementary to first and second nonoverlapping segments of a target sequence. The first and second nonoverlapping segments of the target sequence preferably, respectively, contain first and second polymorphic sites to which (I) and (II) are respectively complementary to. R1 preferably bears (I) with a third probe (III) and R2 preferably bears (II) with a fourth probe (IV), so R1, R2 and R3 comprise three pools of polynucleotide probes. The pools of probes preferably comprise first and second subsets, where in the first subset each pool has a common (I) and a different (II), and in the second subset, each pool has a common (I), different to that in the first subset, and a different (II). Preparation: Arrays or probes can be synthesized in a step-by-step manner on a support or can be attached in presynthesized form. A preferred method of synthesis is VLSIPS (RTM) (Fodor et al., 1991, Fodor et al., 1993, Nature 364, 555-556; McGall et al., USSN 08/445,332; US 5,143854; EP 476,014), which entails the use of light to direct synthesis of oligonucleotide probes in high density.

The basic VLSIPS1 (RTM) approach can readily be adapted to synthesize pooled mixtures of probes. The component probes of a pool are synthesized in series. Synthesis of a pooled probes starts with a substrate covered with a photosensitive protective group. The group is partially removed by

limited exposure of substrate to light. The deprotected sites are capped with a protective group that is nonphotosensitive but can be removed by other means, such as a chemical solvent. The remaining sites are then exposed to more light removing the remaining photosensitive protective groups. Synthesis proceeds on the exposed sites in a step-by-step fashion until first members of pooled probes are synthesized. The nonphotosensitive capping groups are then removed. Synthesis proceeds anchored from these sites in a step-by-step fashion until second members of pooled probes are formed. After hybridization of control and target samples to an array containing one or more probe sets and optional washing to remove unbound and **nonspecifically bound** probe, the hybridization intensity for the respective samples is determined for each probe in the array. For fluorescent labels, hybridization intensity can be determined by, for example, a scanning confocal microscope in photon counting mode.

ABEX

EXAMPLE - To examine the strength and specificity of linkage over a greater distance, paired probe arrays were synthesized with the probe sequences chosen from different regions of a 2.5 kilobase (kb) mitochondrial DNA amplicon. The length of probes was increased to 30-mers to allow hybridizations to be performed under stringent conditions. Higher stringency was used to reduce the secondary structure in the targets and to favor cooperative hybridization by destabilizing individual hybridizations.

Arrays of three different designs were synthesized. In each design a different pair of single nucleotide polymorphisms (SNPs) was interrogated. In each of three experiments, a 50:50 mixture of two 2.5 kb target amplicons was analyzed on a paired array. The two 2.5 kb amplicons are from the identical region of human mitochondrial DNA, but are polymorphic and differ from each other at the specific sites analyzed by the arrays. In the first experiment, SNPs at positions 1438 and 2131 (sequence not given in the specification), separated by 693 nucleotides, were analyzed. The second experiment queried SNPs 1345 nucleotides apart, at positions 93 and 1438. The third experiment queried SNPs 2098 nucleotides apart, at positions 93 and 2131. In each experiment, the correct probe cells have the highest intensity. The results showed single base mismatch discrimination and linkage detection between loci separated by distances up to 2.1 kb, although the discrimination was better with the 9-mer paired probe array. This is not surprising, as the discrimination is based on differences of 2 bases out of 50, as opposed to 2 bases out of 18 in the 9-mer experiments.

The data was then analyzed by comparing each probe pair to its 6 single base alterations (the 3 single base changes in Probe 2, keeping Probe 1 constant, and the 3 single base changes in Probe 1, keeping Probe 2 constant). In this analysis, the distinction between the correct linkage assignments and the incorrect ones was even more apparent. A score of 1 on the discrimination chart meant the intensity at that position on the array was the same as the average intensity of all its one base alterations. All of the incorrect linkage assignments are close to or less than 1, while the correct linkage assignments produce values of 1.8 or greater. As with the 9-mer paired probe array, the correct linkage assignments were easily distinguished from the incorrect phase.

L98 ANSWER 7 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-100772 [09] WPIX
DNC C2000-029763
TI A reagent for nucleic acid amplification and a sequence-specific nucleic acid amplification - used to inhibit **nonspecific** reactions to improve sensitivity and signal.
DC B04 D16
IN KONDO, M; SEGAWA, M; TAKARADA, Y
PA (TOYM) TOYOBO KK; (TOYM) TOYO BOSEKI KK
CYC 2

PI JP 11318473 A 19991124 (200009)* 10p C12N015-09 <--
US 6261773 B1 20010717 (200142) C12Q001-68 <--
ADT JP 11318473 A JP 1999-18434 19990127; US 6261773 B1 US 1999-268710 19990316
PRAI JP 1998-66988 19980317
IC ICM **C12N015-09; C12Q001-68**
ICS **C12P019-34**
AB JP 11318473 A UPAB: 20000218
NOVELTY - A reagent for nucleic acid amplification containing at least one substance selected from EDTA, nitrilotriacetic acid, uramildiacetic acid, trans-1,2-cyclohexanediaminetetraacetic acid, diethylenetriaminepentaacetic acid, ethylene glycol bis(2-aminoethyl)ether diaminetetraacetic acid and triethylenetetraminehexaacetic acid and their salts, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a reagent for nucleic acid amplification containing the above reagent for nucleic acid amplification and a probe for detection; and (2) a method for the sequence-specific nucleic acid amplification in which at least one of the above substances or its salt is added to the reaction liquor of nucleic acid amplification.
USE - The method can be used to inhibit **nonspecific** reactions to improve sensitivity and signal.
ADVANTAGE - The method can easily inhibit **nonspecific** reactions to improve sensitivity and signal.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-E05; B11-C08E; B12-K04F; D05-H12D1; D05-H18B

L98 ANSWER 8 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-055286 [05] WPIX
DNC C2000-014611
TI Modified thermostable enzymes, useful for nucleic acid amplification.
DC B04 D16
IN IVANOV, I; KANG, J; LOEFFERT, D; RIBBE, J; STEINERT, K
PA (QIAG-N) QIAGEN GMBH
CYC 27
PI EP 962526 A2 19991208 (200005)* EN 16p C12N009-99
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000004878 A 20000111 (200013) 16p C12N009-12
US 6183998 B1 20010206 (200109) C12P019-34 <--
ADT EP 962526 A2 EP 1999-110426 19990528; JP 2000004878 A JP 1999-147618 19990527; US 6183998 B1 CIP of US 1998-86846 19980529, US 1998-183950 19981031
PRAI US 1998-183950 19981031; US 1998-86846 19980529
IC ICM C12N009-12; C12N009-99; **C12P019-34**
ICS C07K001-00; **C12N015-09; C12Q001-68**
ICI C12N009-12; C12R001:01
AB EP 962526 A UPAB: 20000128
NOVELTY - A modified thermostable enzyme (I) produced by a reaction (II) under aqueous conditions, of a thermostable enzyme (III) and a modifier reagent (IV) at a temperature of less than 50 deg. C, is new. The modifier reagent is an aldehyde and the reaction results in thermally reversible inactivation of the enzyme.
DETAILED DESCRIPTION - A modified thermostable enzyme (I) produced by a reaction (II) under aqueous conditions, of a thermostable enzyme (III) and a modifier reagent (IV) at a temperature of less than 50 deg. C, is new. The modifier reagent is an aldehyde and the reaction results in thermally reversible inactivation of the enzyme. (II) has the following formula:
RHC = O, where:
R = H or an alkyl, aryl, or alkylaldehyde group of 1 to 10 carbon

atoms.

INDEPENDENT CLAIMS are also included for the following:

(1) a polymerase chain reaction (PCR) amplification reaction mixture (V), comprising (I) and a set of polymerase chain reaction specific primers;

(2) a reagent kit (VI) for performing PCR, comprising (I); and

(3) a method (A) for the amplification of a target nucleic acid, comprising contacting the nucleic acid with (V) under the conditions of (II).

USE - (I), (V), (VI) and (VII) are used for the amplification of a target nucleic acid (claimed), achieved by the chemical modification and reversible inactivation of thermostable enzymes.

ADVANTAGE - The use of (I) in nucleic acid amplification overcomes difficulties associated with **non-specific** amplification products caused by the extension of mis-primed oligonucleotides during the initial heating phase or reaction set-up of PCR. Previous techniques, such as the manual hot-start PCR method and the solid wax barrier method, carry a higher risk of contamination and are time consuming. Here, (I) becomes active only after incubation of the DNA polymerase at a certain elevated temperature, preventing the production of **non-specific** DNA products during the reaction set-up and heating phase, using fewer handling steps.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-B04M; B04-E01; B04-F10; B04-L04A; B04-L04B; B04-M01; B11-C08E3; D05-C07; D05-H12D1; D05-H17B3; D05-H18B; D05-H19B

TECH UPTX: 20000128

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (II) is carried out in the presence of 0.01M to 2M, preferably 20mM to 1M modifier reagent. In (A), the thermostable enzyme is prepared by a reaction of the polymerase in the presence of 0.01M to 2M modifier reagent at a temperature of less than 50degreesC, preferably 37degreesC for 30 minutes. Incubation of (I) at a temperature of at least 50degreesC results in at least a two-fold increase in enzyme activity.

Preferred Enzyme: (III) is preferably a DNA polymerase, derived from Thermus, Pyrrococcus or Thermotoga organisms, preferably T. thermophilus, T. flavus, P. furiosus, P. woesei, P. spec. (strain KOD1) P. spec. OT3 (horikoshii), P. profundus, T. stetteri, T. spec. AN1 (zilligii), T. peptonophilus, T. celer and T. fumicolans. In (A), the polymerase can also be derived from P. spec. GB-D, T. litoralis, T. sp. 9degreesN-7, T. maritima and P. spec. ES4 (endeavori), but is especially derived from Thermus aquaticus.

Preferred Reaction Mixture: (V) and (VI) also comprise a PCR additive which affects the melting behaivour of a nucleic acid, selected from multifunctional polyols, amides, alkaline ammonia salts, sulfoxides, sulfates, SSB proteins, calf thymus protein UP1, glycerol, formamide, tetramethylammonium chloride, dimethylsulfoxide, polyethylene glycol, E. coli SSB protein and T4 gene 32 protein or preferably betaine. (V) also preferably comprises a reverse transcriptase RNase H positive/negative and a nucleic acid, preferably a ribonucleic acid.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Reagent: (IV) is a water soluble aldehyde capable of forming crosslinks between amino-functional side chains of enzyme amino acids, preferably formaldehyde.

ABEX

EXAMPLE - Taq DNA polymerase was modified in a buffer containing 200mM KCL, 1mM EDTA, 20mM HEPES and pH7.9 at enzyme concentrations of 10 to 20 U/mul. Immediately before use, 100mul of formaldehyde was diluted with 168mul of distilled water to produce a stock solution. Different amounts of this were mixed with 4ml of Taq DNA polymerase to achieve varying end concentrations of formaldehyde. The mixture was incubated for 30mm at 37degreesC, followed by quick chilling on ice and removing residual

formaldehyde by gel filtration or ultrafiltration. To stabilize the complex, the modified enzyme was dialyzed against a storage buffer containing 100mM KCL, 0.1mM EDTA, 0.5% (v/v) Tween 20, 0.5% (v/v) Nonidet P40, 1mM DTT, 10mM ethanolamine, 50% glycerol, 20mM Tris/Cl and pH 9.0.

their pub n.

L98 ANSWER 9 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 2000-013271 [01] WPIX
DNN N2000-010276 DNC C2000-002542
TI Method for reducing **nonspecific binding** of target molecule to immobilized array of oligonucleotide probes, useful in diagnosis and drug screening.
DC A96 B04 D16 S03
IN GOLDBERT, M; MCGALL, G; RYDER, T B; WOODMAN, S; GOLDBERG, M
PA (AFFY-N) AFFYMETRIX INC; (GOLD-I) GOLDBERG M; (MCGA-I) MCGALL G; (RYDE-I) RYDER T B; (WOOD-I) WOODMAN S
CYC 87
PI WO 9954509 A1 19991028 (200001)* EN 63p C12Q001-68 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9936591 A 19991108 (200014)
EP 1071821 A1 20010131 (200108) EN C12Q001-68 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2001049108 A1 20011206 (200203) C12Q001-68 <--
JP 2002512045 W 20020423 (200243) 74p C12Q001-68 <--
ADT WO 9954509 A1 **WO 1999-US8745 19990420**; AU 9936591 A AU 1999-36591 19990420; EP 1071821 A1 EP 1999-918749 19990420, **WO 1999-US8745 19990420**; US 2001049108 A1 Cont of US 1998-63311 19980420, US 2001-862571 20010523; JP 2002512045 W **WO 1999-US8745 19990420**, JP 2000-544837 19990420
FDT AU 9936591 A Based on WO 9954509; EP 1071821 A1 Based on WO 9954509; JP 2002512045 W Based on WO 9954509
PRAI US 1998-63311 19980420; US 2001-862571 20010523
IC ICM **C12Q001-68**
ICS C07H021-02; C07H021-04; **C12N015-09**; **C12P019-34**; G01N033-53; G01N033-566
AB WO 9954509 A UPAB: 20000105
NOVELTY - Methods for reducing **nonspecific binding** of a target molecule (I) to an array of polynucleotide probes (II) on a solid support.

DETAILED DESCRIPTION - The methods comprise:

(1) removing protecting groups (PG) from some known locations on the support surface;

(2) forming (II), containing a terminal PG, at these locations, and replacing PG, on (II) and/or those remaining on the support, with a negatively charged phosphate residue (A);

(3) attaching a polyanionic chain (PAC) to many known locations on the support, then forming (II) on each PAC;

(4) attaching PAC outside the known locations, then forming (II) at the known locations;

(5) as in (1), but forming PAC with a PG at the known locations, forming (II), having a terminal PG on PAC and removing terminal PG in (II) and/or residual PG on the support;

(6) as in (3) but where PAC carry a PG, and removal of PG from (II) and/or from the support outside the known locations;

(7) forming PAC at known locations, forming (II) with terminal PG on PAC at these locations, and replacing PG, on the probes and/or those outside the known locations, with (A);

(8) forming a PAC, with PG, outside known locations, forming (II) with PG, at the known locations, then replacing PG on (II), or those

outside the known locations, with (A).

An INDEPENDENT CLAIM is also included for screening (I) for hybridization to an array of (II) in which the array carries PAC, outside and/or within, the known locations, and (II) are attached through PAC at the known locations.

USE - The method is used to produce arrays for determining **binding** affinity, for drug screening and diagnosis.

ADVANTAGE - Suppression of **nonspecific binding** improves the accuracy of qualitative and quantitative measurements of (I).

Dwg.0/3

FS CPI EPI

FA AB; DCN

MC CPI: A12-V03C2; A12-W11L; B04-B03C; B04-E05; B11-C07A6; B11-C08E5; B12-K04; B12-K04E; B12-K04F; D05-H09; D05-H10; D05-H12; D05-H12D1

EPI: S03-E14H4

TECH UPTX: 20000105

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred supports: These are polymerized Langmuir-Blodgett films, functionalized glass, germanium, silicon, polymers, gallium arsenide and/or metal oxides. They may be flat or patterned to include wells and channels.

Preferred methods: In method (1), a linker monomer, having a photolabile PG (pPG) is attached at each known location, then monomers, each with a pPG, attached in sequence to form a probe having terminal pPG. Alternatively, the monomers contain chemically removable PG which are replaced by pPG before the next round of synthesis. Terminal PG are removed by treatment with an activator (acid, base, oxidant or reductant) and the resulting activated group is reacted with a compound (B) that attaches (A) to probe or support or a monomer (C) having a negatively charged phosphate unit and PG, with this step repeated 1-20 times to create PAC. Preferably PG are removed from both probes and support. In method (2), PAC are constructed from (C) by standard sequential reactions at known locations, with each (C) being activated (as above or by radiation) before the next round. The other methods use basically the same techniques.

TECHNOLOGY FOCUS - POLYMERS - Suitable polymers for the support are poly(tetrafluoroethylene) and polystyrene.

ABEX

WIDER DISCLOSURE - A support for solid-phase synthesis in which a PAC, with PG, is attached to (i) designated regions of a support and/or (ii) protected regions is also disclosed as new.

EXAMPLE - A silane-activated glass wafer was reacted 1 to 8 times with 3-(DMToxy)propyl-(2-cyanoethyl)-N,N-di-isopropylphosphoramidite (DMT = dimethoxytrityl), to introduce a C3 spacer, with (DMT-hexaethyloxy)phosphorimidate to introduce a hexaethoxy (HEX) linker and with 5'-O-MeNPOC-(N-2-p-isopropylphenoxyacetyl)-2'-deoxyguanosine-3'-O-(2-cyanoethyl)-N,N-di-isopropylphosphoramidite (MeNPOC = 2-methyl-2-(2-nitrophenyl)ethoxycarbonyl). The support was exposed to ultraviolet light through a mask to create a pattern of activated and protected regions and synthesis of a 20-mer oligonucleotide carried out by conventional sequential reaction on the activated regions, using MeNPOC-protected reactants. The oligonucleotide formed was reacted with its biotinylated complement, then this was reacted with a phycoerythrin-streptavidin complex and the fluorescence measured. The signal-to-noise ratio was 28 when the support carried a HEX linker only (fluorescent intensities 9650 and 348 (background)) but for the derivatized support having m = 5, the ratio was 364 (intensities 20035 and 55).

L98 ANSWER 10 OF 32 WPIX (C) 2003 THOMSON DERWENT

AN 1999-494540 [41] WPIX

DNC C1999-145052

TI Performing nucleic acid extension reaction in presence of osmoprotectant,

e.g. proline, particularly for sequencing and amplification - increases stability of polymerase and reduces melting temperature of template or primer.

DC B03 B04 D16

IN IAKOBASHVILI, R; LAPIDOT, A; MALIN, G

PA (YEDA) YEDA RES & DEV CO LTD

CYC 23

PI WO 9941410 A1 19990819 (199941)* EN 49p C12Q001-68 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA IL JP US
EP 1053350 A1 20001122 (200061) EN C12Q001-68 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002503482 W 20020205 (200212) 55p C12Q001-68 <--
US 6428986 B1 20020806 (200254) C12P019-34 <--

ADT WO 9941410 A1 WO 1999-IL80 19990208; EP 1053350 A1 EP 1999-903891 19990208, WO 1999-IL80 19990208; JP 2002503482 W WO 1999-IL80 19990208, JP 2000-531590 19990208; US 6428986 B1 WO 1999-IL80 19990208, US 2000-601943 20000810

FDT EP 1053350 A1 Based on WO 9941410; JP 2002503482 W Based on WO 9941410; US 6428986 B1 Based on WO 9941410

PRAI IL 1998-123256 19980210

IC ICM **C12P019-34; C12Q001-68**
ICS **C12N015-09**

AB WO 9941410 A UPAB: 19991011

NOVELTY - A cycled primer extension reaction comprises:

(i) treating template DNA, with at least one primer (I) that anneals to the 3'-end of TS in presence of an osmoprotectant (II) to lower the melting temperature (Tm) of template and/or primer, and

(ii) polymerase-mediated extension of annealed (I) in presence of (II), to stabilize the polymerase and provide high yield, specific extension.

DETAILED DESCRIPTION - A cycled primer extension reaction comprises:

(i) treating template DNA, that includes a target sequence (TS), with at least one primer (I) that anneals to the 3'-end of TS in presence of an osmoprotectant (II) to lower the melting temperature (Tm) of template and/or primer, and

(ii) polymerase-mediated extension of annealed (I) in presence of (II), to stabilize the polymerase and provide high yield, specific extension. (II) is proline and/or 2-methyl-4-carboxy-3,4,5,6-tetrahydropyrimidine (IIa).

INDEPENDENT CLAIMS are also included for the following:

(a) method for lowering Tm of a double-stranded DNA by incubating in presence of (IIa);

(b) method for stabilizing DNA polymerase at high temperature by addition of proline and/or (IIa); and

(c) kits for sequencing or amplifying DNA comprising usual sequencing/amplification reagents and proline and/or (IIa).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The extension reaction is specifically an amplification or sequencing reaction, used e.g. for diagnosis or screening of genetic diseases or cancer; for rapid detection of mycobacteria or human immune deficiency virus; for detecting minimal residual disease in leukemia or for HLA typing, but also in forensic pathology and evolutionary biology.

ADVANTAGE - (II) increase stability of DNA polymerase and/or reduce melting temperature (Tm), resulting in improved specificity and yield, particularly when using GC-rich targets for which reduction in Tm is greatest. The amount of polymerase may be reduced and/or polymerases of lower thermal stability (usually more accurate), also heat-labile labels, can be used. This eliminates formation of **non-specific** products (allowing detection of rare mutations or multiple repeats of CGG encountered in Huntington's disease) and makes possible an increase in the number of reaction cycles or of cycle times. In a typical case, the

half-live at 65 deg. C of Klenow fragment was 30-50 sec, but this was increased to 25 min in presence of 5 M proline.
Dwg.0/14
FS CPI
FA AB; DCN
MC CPI: B04-E01; B04-E05; B07-D03; B11-C01; B11-C08E4; B12-K04F; D05-H18B
TECH UPTX: 19991105
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred process: Steps (i) and (ii) are repeated many times, with each step (i) being preceded by denaturation, at a temperature at which the polymerase is stable, to separate the template into its strands and to separate the extended primer for its complement. In a sequencing reaction, extension is performed in presence of all four deoxynucleotide triphosphates (dNTP) and of a small amount of one dideoxynucleotide triphosphate (ddNTP). Optionally deoxyguanosine triphosphate is replaced by its 7-deaza analog. In an amplification process, specifically polymerase chain reaction, two primers, complementary to the 3'-ends of both strands, are used. Particularly the template is rich in GC and the polymerase may be heat-stable (e.g. Taq, Klentaq 1 or Pfu) or not heat-stable (e.g. T7, T4, Klenow fragment, reverse transcriptase, Bca, Bst or their mutants). Typically (II) is used at 0.5-1.5 M for DNA of average GC content or 1-3 M for GC-rich DNAs. When (II) is used at a high concentration, primers have at least 30 nucleotides
ABEX
EXAMPLE - Genomic DNA of Halobacterium marimortui, 66.5% GC, was amplified with two 28-mer primers (sequences reproduced) by an essentially standard polymerase chain reaction with Taq polymerase. 35 cycles were performed, each of (i) 30 sec at 92 or 95 degreesC; (ii) 90 sec at 55 degreesC and (iii) 60 sec at 72 degreesC, in absence or presence of 0.5 M 2-methyl-4-carboxy-3,4,5,6-tetrahydropyrimidine (IIa). At both denaturation temperatures (IIa) increased the yield and specificity of DNA amplification; at 92 degreesC no amplification was detected in absence of (IIa).

L98 ANSWER 11 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1999-205980 [18] WPIX
DNC C1999-060184
TI Hybridisation-independent nucleic acid synthesis and amplification - by polymerase-catalysed reaction initiated by **nonspecific** oligonucleotide.
DC B04 D16
IN EHRICHT, R; ELLINGER, T
PA (MOLE-N) INST MOLEKULARE BIOTECHNOLOGIE EV
CYC 82
PI DE 19741714 A1 19990325 (199918)* 15p C12P019-34 <--
WO 9915698 A2 19990401 (199920) DE C12Q001-68 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9897452 A 19990412 (199934) C12Q001-68 <--
EP 1015640 A2 20000705 (200035) DE C12Q001-68 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU MC NL PT SE
JP 2001517458 W 20011009 (200174) 34p C12N015-09 <--
DE 19741714 C2 20020321 (200222) C12P019-34 <--
ADT DE 19741714 A1 DE 1997-19741714 19970922; WO 9915698 A2 WO 1998-EP6006 19980921; AU 9897452 A AU 1998-97452 19980921; EP 1015640 A2 EP 1998-951443 19980921, WO 1998-EP6006 19980921; JP 2001517458 W WO 1998-EP6006 19980921, JP 2000-512986 19980921; DE 19741714 C2 DE 1997-19741714 19970922
FDT AU 9897452 A Based on WO 9915698; EP 1015640 A2 Based on WO 9915698; JP

2001517458 W Based on WO 9915698
PRAI DE 1997-19741714 19970922
IC ICM **C12N015-09; C12P019-34; C12Q001-68**
ICS C07H021-00; C07K001-00
AB DE 19741714 A UPAB: 19990511
NOVELTY - A method (I) for synthesising and optionally amplifying nucleic acids, comprising a polymerase-catalysed reaction that is hybridisation-independent and is initiated by at least one nucleic acid that is single-stranded at least at the 3' end. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid molecule produced by the above method; (2) an intermediate product formed in the above method (especially a complex of at least one nucleic acid and at least one polymerase enzyme); (3) a protein molecule that has been produced using the above method, ''as well as a corresponding gene''; and (4) a method (II) stated to be as above where the starting template is a single-stranded nucleic acid and the hybridisation-dependent reaction step is preceded by hybridisation of a complementary initiator nucleic acid to the 3' end of the template and polymerase-catalysed second strand formation.

USE - The new method (I) is useful for copying or amplifying total DNA or random sequences e.g. to produce shuffled DNA sequences or random oligonucleotides, or to produce non-sequence-specific nucleic acid fusions. Method (II) is useful for transcribing RNA into double-stranded DNA with simultaneous amplification.

ADVANTAGE - Synthesis and amplification can be achieved without the need for hybridisation of complementary oligonucleotide primers to the nucleic acid.

Dwg.0/5
FS CPI
FA AB
MC CPI: B04-E01; B04-L04A; B04-N04; B11-C08E3; D05-H12A; D05-H17; D05-H18B

L98 ANSWER 12 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1998-570547 [49] WPIX
DNC C1998-171609
TI Detecting target nucleotide sequences e.g. HIV-1 and M. tuberculosis in a specimen sample - by amplifying and detecting target sequence using a labelled analyte-specific material in a gel matrix.
DC B04 D15 D16 J04
IN LEVINE, R A; WARDLAW, S C
PA (LEVI-I) LEVINE R A; (WARD-I) WARDLAW S C; (WARD-N) WARDLAW PARTNERS LP
CYC 32
PI EP 877094 A2 19981111 (199849)* EN 29p C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 9801923 A 19981030 (199902) C12Q001-68 <--
FI 9800925 A 19981030 (199904) C12Q000-00
AU 9852891 A 19981105 (199905) G01N033-68
JP 10304898 A 19981117 (199905) 19p C12Q001-68 <--
CA 2222909 A 19981029 (199914) C12Q001-68 <--
CN 1209546 A 19990303 (199928) G01N033-00
US 6007990 A 19991228 (200007) C12Q001-68 <--
MX 9802123 A1 19990101 (200051) G01N033-532
AU 733385 B 20010510 (200130) G01N033-68
CA 2222909 C 20020129 (200211) EN C12Q001-68 <--
ADT EP 877094 A2 EP 1998-107881 19980429; NO 9801923 A NO 1998-1923 19980428; FI 9800925 A FI 1998-925 19980427; AU 9852891 A AU 1998-52891 19980204; JP 10304898 A JP 1998-72379 19980320; CA 2222909 A CA 1998-2222909 19980205; CN 1209546 A CN 1998-107777 19980428; US 6007990 A US 1997-841267 19970429; MX 9802123 A1 MX 1998-2123 19980318; AU 733385 B AU 1998-52891 19980204; CA 2222909 C CA 1998-2222909 19980205
FDT AU 733385 B Previous Publ. AU 9852891
PRAI US 1997-841267 19970429

IC ICM C12Q000-00; **C12Q001-68**; G01N033-00; G01N033-532; G01N033-68
ICS **C12N015-09**; **C12P019-34**; G01N033-58
ICA C12Q001-70
ICI C12N015-09, C12R001:92; C12N015-09, C12R001:32; C12N015-09, C12R001:01; C12N015-09, C12R001:445
AB EP 877094 A UPAB: 19981210
Determining the presence or absence of a target nucleotide sequence analyte (target analyte) in a specimen sample by amplifying target and reacting with a detectable substance is new. Also claimed are: (1) a method of quantifying a target sequence in a specimen sample by amplifying target sequence and reacting with a labelled analyte-specific material (LASM); (2) a method of determining and quantifying at least two target nucleotide sequences in a specimen sample by amplifying target sequence and reacting with LASMs; and (3) an assembly for determining the presence or absence of one or at least two target nucleotide sequences in a sample using amplification reagents and a detection substance or LASMs respectively.
USE - The new method is useful for detecting protozoa, bacteria, virus and fungi organisms (e.g. HIV-1 and M. tuberculosis) in water and food samples, and in biological samples including blood, tissue, urine, stools and cerebrospinal fluid. The cause of a disease can be determined in one test by having a number of different specific amplification primers and LASMs.
ADVANTAGE - The new method can specifically determine and quantify the presence or absence of at least one nucleotide sequence (DNA or RNA) in a few hours, compared to prior art methods which had **non-specific** detection procedures which can only detect one RNA (not DNA) target at one time, taking from one day to weeks.
FS CPI
FA AB
MC CPI: B04-B04B1; B04-B04D5; B04-B04H; B04-E05; B04-F10B2; B04-F11; B11-C08E5; B12-K04A4; B12-K04F; D05-H04; D05-H05; D05-H06; D05-H09; D05-H18B; J04-B01

L98 ANSWER 13 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1998-559447 [48] WPIX
CR 2002-438026 [47]
DNC C1998-167627
TI Automated nucleic acid hybridisation assay - used to detect e.g. Mycobacterium tuberculosis, Chlamydia trachomatis, Neisseria gonorrhoeae and HIV.
DC B04 D16
IN BURG, J L; CATANZARITI, L; KLUTTZ, B W; MCKINLEY, G A; MOE, J G; VERA-GARCIA, M; BURG, L J; CATANZARIT, L; GARCIA, M V
PA (INMR) BIOMERIEUX VITEK INC
CYC 32
PI EP 875584 A2 19981104 (199848)* EN 60p C12Q001-68 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 9863766 A 19981105 (199905) C12Q001-68 <--
JP 10304890 A 19981117 (199905) 38p C12N015-09 <--
CA 2230967 A 19981102 (199915) C12P019-34 <--
BR 9801572 A 19990629 (199937) C12N015-11
KR 98086701 A 19981205 (200009) C12Q001-68 <--
MX 9803500 A1 19990201 (200055) G01N035-00
US 6300068 B1 20011009 (200162) C12Q001-68 <--
AU 2001058009 A 20011018 (200174)# C12Q001-68 <--
ADT EP 875584 A2 EP 1998-303458 19980501; AU 9863766 A AU 1998-63766 19980501; JP 10304890 A JP 1998-123564 19980506; CA 2230967 A CA 1998-2230967 19980501; BR 9801572 A BR 1998-1572 19980504; KR 98086701 A KR 1998-15754 19980501; MX 9803500 A1 MX 1998-3500 19980430; US 6300068 B1 Div ex US 1997-850171 19970502, US 1999-245939 19990205; AU 2001058009 A Div ex AU 1998-63766 19980501, AU 2001-58009 20010814

PRAI US 1997-850171 19970502; US 1999-245939 19990205; AU 2001-58009 20010814

IC ICM **C12N015-09**; C12N015-11; **C12P019-34**; **C12Q001-68**; G01N035-00
ICS B01L001-00; C07H021-00; C12M001-18; C12M001-34; C12M001-40; C12Q001-70; G01N033-68

ICI C12Q001-68, C12R001:32; C12Q001-68, C12R001:01; C12Q001-68, C12R001:36; C12Q001-68, C12R001:92

AB EP 875584 A UPAB: 20020725

A unified buffer for an isothermal amplification assay for denaturation of double-stranded nucleic acids and for annealing of nucleic acids, which is further capable of sustaining the activity of a nucleic acid polymerisation enzyme, comprising a sample dilution buffer, amplification reconstitution buffer and enzyme dilution buffer, is new. Also claimed are: (i) generation of a universal positive amplification internal control nucleic acid, comprising generating random nucleic acid sequences of at least ten nucleotides in length, screening them and selecting for specific functionality, combining in tandem more than one such selected nucleic acid, screening the combined nucleic acid sequences and optionally selecting against formation of intra-strand nucleic acid dimers or formation of hairpin structures; (ii) a universal positive amplification internal control nucleic acid sequence comprising a nucleic acid sequence which is randomly generated; (iii) detection of the presence or absence of a single-stranded or double-stranded first nucleic acid in a sample by automated isothermal amplification of the first nucleic acid in a dual chamber reaction vessel comprising first and second reaction chambers, which may be placed in fluid communication with each other such that the fluid communication may be controllably interrupted, comprising combining the sample, a reaction buffer, a mixture of free nucleotides and first and second specific oligonucleotide primers in the first reaction chamber and placing the reaction vessel in an automated apparatus such that the automated apparatus heats the first reaction chamber to a sufficient temperature and for a sufficient time to render any double-stranded first nucleic acid in the sample to be tested into sufficient single-stranded nucleic acid such that a hybridisation product may form, the hybridisation product comprising the first nucleic acid and at least one of the first and second oligonucleotide primers, the automated apparatus then cools the first reaction chamber to a sufficient temperature such that the hybridisation product forms, if the first nucleic acid is present, the automated apparatus then transfers the reaction mixture from the first reaction chamber to the second reaction chamber via the controllable fluid communication such that the reaction mixture is brought into contact with a nucleic acid polymerisation enzyme, the automated apparatus maintains the second reaction chamber at a sufficient temperature which allows for the specific oligonucleotide primer mediated amplification of the first nucleic acid, if present, the automated apparatus then contacts any amplicon product from the first nucleic acid in the second reaction chamber with a capture nucleic acid specific for the amplicon from the first nucleic acid such that a specifically **bound** nucleic acid-capture probe hybridisation complex may form, the automated apparatus optionally washes the hybridisation complex mixture such that **non-specifically bound** nucleic acid is washed away from the specifically **bound** nucleic acid-capture probe complex, the automated apparatus contacts the specifically **bound** nucleic acid-capture probe complex with a labelled nucleic acid probe specific for the amplicon produced from the first nucleic acid such that a specifically-**bound** nucleic acid-capture probe-labelled probe complex may form, the automated apparatus optionally washes the specifically **bound** nucleic acid-capture probe-labelled probe complex such that **non-specifically bound** labelled probe nucleic acid is washed away from the specifically **bound** nucleic acid-capture probe-labelled probe complex and the automated apparatus detects the presence or absence of the generated

signal and optionally displays a value for the signal, and optionally records a value for the signal, the automated apparatus contacting the specifically-**bound** nucleic acid-capture probe-labelled probe complex with a solution such that a detectable signal is generated if the amplicon and first nucleic acid are present, the signal generated from the sample being proportional to the amount of the first nucleic acid in the sample, each of the three last steps being performed sequentially or concurrently; (iv) specific automated detection of one or more viral or microbial nucleic acids in a sample comprising lysing at least one microorganism in the sample, if present, to liberate target nucleic acid, amplifying the nucleic acid to form amplicons, contacting the sample with a solid phase receptacle coated with a capture nucleic acid, such that the capture nucleic acid may form a hybridisation complex with the amplicons, allowing the hybridisation complex to form, contacting it with a detection nucleic acid, such that the detection nucleic acid may form a specific hybridisation detection complex with the amplicon, and is conjugated to a means for generating a detectable signal selected from an enzyme, chromophore chemiluminescent compound, radioisotope and fluorophore, allowing the detection complex to form and generating the detectable signal, detecting the detectable signal if the amplicon is present in the sample and optionally, between operations, the hybridisation complex may be washed to remove excess **non-specifically bound** nucleic acid; (v) a device for the automated detection of a first target nucleic acid and a second target nucleic acid, comprising a solid phase receptacle which is coated with a first capture nucleic acid which may form a specific hybridisation complex with the first nucleic acid and a second capture nucleic acid which may form a specific hybridisation complex with the second nucleic acid; and (vi) automated detection of the presence or absence of a first target nucleic acid and a second target nucleic acid in a sample, comprising contacting the sample with a solid phase receptacle as in (v), allowing a specific hybridisation complex to form if the nucleic acid is present, contacting the solid phase receptacle hybridisation complex with a first detection nucleic acid, which may form a specific hybridisation detection complex with the first nucleic acid and is conjugated to a means for generating a detectable signal selected from an enzyme, chromophore, chemiluminescent compound, radioisotope and fluorophore, allowing a specific detection complex to form and then generating the detectable signal, detecting the signal if the first nucleic acid is in the sample, contacting the solid phase receptacle hybridisation complex with a second detection nucleic acid which may form a specific hybridisation detection complex with the second nucleic acid and is conjugated to a means for generating a detectable signal selected from enzyme, chromophore, chemiluminescent compound, radioisotope and fluorophore, allowing a specific detection complex to form and then generating the detectable signal, detecting the signal if the second nucleic acid is in the sample, optionally between operations the hybridisation complex being washed to remove excess **non-specifically bound** nucleic acid and the absence of a detectable signal correlating with the absence of the nucleic acid in the sample.

USE - Process (iv) is useful for detecting Mycobacterium tuberculosis, Chlamydia trachomatis, Neisseria gonorrhoeae or Human Immunodeficiency Virus (HIV) and process (vi) is useful for detecting Chlamydia trachomatis and Neisseria gonorrhoeae.

Dwg.0/30

FS CPI
FA AB
MC CPI: B04-E05; B04-F10A; B04-F10B2; B04-F11; B11-C08E5; B12-K04A4; B12-K04F; D05-A01A4; D05-A01B; D05-H04; D05-H06; D05-H09; D05-H12D1

L98 ANSWER 14 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1998-482929 [42] WPIX
DNC C1998-146155

TI Oligo-nucleotide(s) containing N-substituted nucleotide - useful as primers for nucleic acid amplification.
DC B04 D16
IN WILL, S G; YOUNG, K K Y
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE MOLECULAR SYSTEMS INC
CYC 36
PI EP 866071 A2 19980923 (199842)* EN 38p C07H021-00
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CZ 9800841 A3 19981014 (199847) C07H021-00
NO 9801239 A 19980921 (199847) C07H021-00
AU 9858404 A 19981001 (199851) C07H019-06
JP 10279593 A 19981020 (199901) 30p C07H021-00
CN 1194270 A 19980930 (199907) C07H021-00
CA 2229766 A 19980920 (199909) C12P019-34 <--
HU 9800581 A2 19990528 (199930) C07H021-00
JP 2966389 B2 19991025 (199950) 30p C07H021-00
AU 712448 B 19991104 (200003) C07H019-06
KR 98080494 A 19981125 (200005) C07H021-50
US 6001611 A 19991214 (200005) C12P019-34 <--
BR 9801878 A 20000919 (200050) C12P019-34 <--
MX 9802007 A1 19990301 (200051) C12P019-30 <--
RU 2159248 C2 20001120 (200108) C07H021-00
CA 2229766 C 20011225 (200210) EN C12P019-34 <--
KR 292997 B 20011217 (200249) C12Q001-68 <--
MX 205092 B 20011108 (200279) C07H021-00
ADT EP 866071 A2 EP 1998-104461 19980312; CZ 9800841 A3 CZ 1998-841 19980319; NO 9801239 A NO 1998-1239 19980319; AU 9858404 A AU 1998-58404 19980313; JP 10279593 A JP 1998-90641 19980320; CN 1194270 A CN 1998-105627 19980319; CA 2229766 A CA 1998-2229766 19980318; HU 9800581 A2 HU 1998-581 19980316; JP 2966389 B2 JP 1998-90641 19980320; AU 712448 B AU 1998-58404 19980313; KR 98080494 A KR 1998-9644 19980320; US 6001611 A Provisional US 1997-41127P 19970320, US 1998-39866 19980316; BR 9801878 A BR 1998-1878 19980320; MX 9802007 A1 MX 1998-2007 19980313; RU 2159248 C2 RU 1998-105786 19980319; CA 2229766 C CA 1998-2229766 19980318; KR 292997 B KR 1998-9644 19980320; MX 205092 B MX 1998-2007 19980313
FDT JP 2966389 B2 Previous Publ. JP 10279593; AU 712448 B Previous Publ. AU 9858404; KR 292997 B Previous Publ. KR 98080494
PRAI US 1997-41127P 19970320; US 1998-39866 19980316
IC ICM C07H019-06; C07H021-00; C07H021-50; **C12P019-30**; **C12P019-34**; **C12Q001-68**
ICS C07H019-16; C07H021-04; **C12N015-09**; G01N033-53; G01N033-58
AB EP 866071 A UPAB: 19981021
Oligonucleotides of formula 5'-S1-Nu-3' or 5'-S1-Nu-S2-3' are new, where S1 is a sequence of 5-50 nucleotides; S2 is a sequence of 1-3 nucleotides; and Nu is a nucleotide with a purine or pyrimidine base having an exocyclic amino group substituted by CHR1R2; R1, R2 are H, 1-10C alkyl, alkoxy, optionally substituted phenyl, phenoxy or optionally substituted naphthyl.
USE - The oligonucleotides are useful as primers for nucleic acid amplification, preferably by polymerase chain reaction.
ADVANTAGE - Use of the modified primers reduces **non-specific** amplification, especially primer dimer formation, with a concomitant increase in the yield of the intended target.
Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-B03C; B04-E05; D05-H12D1; D05-H18B

L98 ANSWER 15 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1998-447254 [38] WPIX
DNC C1998-135767
TI New mutant polymerases that do not add non-templated 3'-nucleotides -

specifically for analysis of hypervariable polymorphisms e.g. for forensic and paternity testing, disease diagnosis.

DC B04 D16

IN CHATTERJEE, D K; SOLUS, J; YANG, S

PA (LIFE-N) LIFE TECHNOLOGIES INC; (CHAT-I) CHATTERJEE D K; (SOLU-I) SOLUS J; (YANG-I) YANG S; (INVI-N) INVITROGEN CORP

CYC 82

PI WO 9835060 A1 19980813 (199838)* EN 186p C12Q001-68 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9863251 A 19980826 (199902) C12Q001-68 <--
EP 986651 A1 20000322 (200019) EN C12Q001-68 <--
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2001511018 W 20010807 (200150) 181p C12Q001-68 <--
US 6306588 B1 20011023 (200165) C12Q001-68 <--
US 2002168646 A1 20021114 (200277) C12Q001-68 <--

ADT WO 9835060 A1 WO 1998-US2791 19980209; AU 9863251 A AU 1998-63251 19980209; EP 986651 A1 EP 1998-907446 19980209, WO 1998-US2791 19980209; JP 2001511018 W JP 1998-535069 19980209, WO 1998-US2791 19980209; US 6306588 B1 Provisional US 1997-37393P 19970207, Provisional US 1998-70562P 19980106, US 1998-19160 19980206; US 2002168646 A1 Provisional US 1997-37393P 19970207, Provisional US 1998-70562P 19980106, Div ex US 1998-19160 19980206, US 2001-891332 20010627

FDT AU 9863251 A Based on WO 9835060; EP 986651 A1 Based on WO 9835060; JP 2001511018 W Based on WO 9835060

PRAI US 1998-70562P 19980106; US 1997-37393P 19970207; US 1998-19160 19980206; US 2001-891332 20010627

IC ICM **C12Q001-68**
ICS A61K035-14; C07K017-00; C12N001-15; C12N001-19; C12N001-21; C12N005-10; C12N009-12; C12N011-16; C12N015-00; **C12N015-09**; C12N015-63; C12N015-85; **C12P019-34**

AB WO 9835060 A UPAB: 19981028
A method for identifying amplification of polymorphic DNA comprises reacting a DNA sample with at least one DNA polymerase (I) having reduced ability to add non-templated nucleotides (nt) to the 3'-terminus, optionally followed by analysis, identification or typing of the amplicons.

Also new are: (1) method for cloning DNA by amplification with (I) and insertion of amplicons in a vector; (2) a polymerase (II) that has been modified or mutated to reduce or eliminate its ability to add non-templated 3'-nt; (3) 43 specific mutant Tne (Thermotoga neopolitana) polymerases e.g. Tne D137A, D323A R722H; Tne D137A, D323A, R722N, F730Y; (4) vectors containing a gene that encodes (II); (5) host cells containing this vector.

USE - Analysis of polymorphic DNA is particularly used to establish relationships between individuals (e.g. forensic or paternity testing), particularly where the polymorphism is a mini- or micro-satellite or short tandem repeat. More generally (I) and (II) are useful in any process that involves nucleic acid amplification, e.g. identification of pathogens, cancer or genetic diseases (e.g. cystic fibrosis, haemophilia, Alzheimer's disease), screening organs or tissues before transplanting, diagnosis, plant breeding.

ADVANTAGE - Since (I) do not add 3'-nt, they provide a more faithful amplification and resolution of polymorphisms, especially in hypervariable regions.

Dwg.0/13

FS CPI

FA AB

MC CPI: B04-E02E; B04-E08; B04-F0100E; B04-L0400E; B12-K04F; D05-H09; D05-H12E; D05-H14; D05-H17B3; D05-H18B; D05-H19B

L98 ANSWER 16 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1997-203356 [19] WPIX
DNC C1997-065187
TI Thermostable enzyme useful in, e.g. nucleic acid amplification methods - is reversibly inactivated by chemical modification, e.g.with citraconic anhydride.
DC B03 B04 D16
IN BIRCH, D E; LAIRD, W J; ZOCCOLI, M A; ZOCCOLI, M A D
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE MOLECULAR SYSTEMS INC
CYC 25
PI

AU 9662179	A	19970313	(199719)*		44p	C12N009-99	
NO 9603541	A	19970226	(199719)			C12N009-12	
EP 771870	A1	19970507	(199723)	EN	26p	C12N009-99	
R: AT BE CH DE DK ES FR GB IT LI NL SE							
JP 09103292	A	19970422	(199726)		19p	C12N009-12	
CA 2184105	A	19970226	(199728)			C12N009-96	
CZ 9602495	A3	19970611	(199730)			C12N015-10	
ES 2101668	T1	19970716	(199735)			C12N009-99	
US 5677152	A	19971014	(199747)		20p	C12P019-34	<--
HU 9602289	A2	19970528	(199803)			C12Q001-68	<--
KR 97010965	A	19970327	(199814)			C12N015-09	<--
MX 9603608	A1	19970301	(199820)			C12N015-52	
AU 689047	B	19980319	(199825)			C12N009-99	
BR 9603563	A	19980519	(199826)			C12N009-99	
US 5773258	A	19980630	(199833)			C12P019-34	<--
EP 771870	B1	19990203	(199910)	EN		C12N009-99	
R: AT BE CH DE DK ES FR GB IT LI NL SE							
DE 69601488	E	19990318	(199917)			C12N009-99	
ES 2101668	T3	19990701	(199933)			C12N009-99	
CA 2184105	C	19990720	(199948)	EN		C12N009-96	
JP 3026554	B2	20000327	(200020)		19p	C12N009-12	
IL 119088	A	20000716	(200049)			C12N009-96	
KR 221097	B1	19991001	(200108)			C12N015-09	<--
MX 195392	B	20000302	(200123)			C12P019-034	<--
CN 1151437	A	19970611	(200132)			C12N009-00	
RU 2174556	C2	20011010	(200175)			C12N009-04	
CZ 289237	B6	20011212	(200203)			C12N009-99	

ADT AU 9662179 A AU 1996-62179 19960821; NO 9603541 A NO 1996-3541 19960823; EP 771870 A1 EP 1996-113222 19960817; JP 09103292 A JP 1996-240996 19960826; CA 2184105 A CA 1996-2184105 19960823; CZ 9602495 A3 CZ 1996-2495 19960823; ES 2101668 T1 EP 1996-113222 19960817; US 5677152 A Provisional US 1995-2673P 19950825, US 1996-684108 19960719; HU 9602289 A2 HU 1996-2289 19960821; KR 97010965 A KR 1996-35291 19960824; MX 9603608 A1 MX 1996-3608 19960823; AU 689047 B AU 1996-62179 19960821; BR 9603563 A BR 1996-3563 19960826; US 5773258 A Provisional US 1995-2673P 19950825, US 1996-680283 19960711; EP 771870 B1 EP 1996-113222 19960817; DE 69601488 E DE 1996-601488 19960817, EP 1996-113222 19960817; ES 2101668 T3 EP 1996-113222 19960817; CA 2184105 C CA 1996-2184105 19960823; JP 3026554 B2 JP 1996-240996 19960826; IL 119088 A IL 1996-119088 19960819; KR 221097 B1 KR 1996-35291 19960824; MX 195392 B MX 1996-3608 19960823; CN 1151437 A CN 1996-113219 19960825; RU 2174556 C2 RU 1996-116815 19960823; CZ 289237 B6 CZ 1996-2495 19960823
FDT ES 2101668 T1 Based on EP 771870; AU 689047 B Previous Publ. AU 9662179; DE 69601488 E Based on EP 771870; ES 2101668 T3 Based on EP 771870; JP 3026554 B2 Previous Publ. JP 09103292; CZ 289237 B6 Previous Publ. CZ 9602495
PRAI US 1995-2673P 19950825; US 1996-684108 19960719; US 1996-680283 19960711
REP 2.Jnl.Ref; EP 655506; US 5262525; WO 8902916; WO 9102090; WO 9109950; WO 9203556; WO 9206200

IC ICM C12N009-00; C12N009-04; C12N009-12; C12N009-96; C12N009-99; **C12N015-09**; C12N015-10; C12N015-52; **C12P019-034**; **C12P019-34**; **C12Q001-68**
ICS C07D307-00; C07K013-00; C07K013-000; C12N009-88; C12N015-11; C12Q001-068; C12Q001-25
ICA C07D307-60
ICI C12N009-12, C12R001:01; C12N009-12, C12R001:01
AB AU 9662179 A UPAB: 19970512
Thermostable enzyme (TE) which is reversibly inactivated by chemical modification, is new. Incubation of the chemically modified TE in an aq. buffer at alkaline pH at < 25 deg. C results in no significant increase in enzyme activity in < 20 mins. Incubation of the chemically modified TE in an aq. buffer, formulated to pH 8-9 at 25 deg. C, > 50 deg. C, results in at least 2-fold increase in enzyme activity < 20 mins.

USE - The modified TE can be used in nucleic acid amplification methods which use a primer based amplification reaction (all claimed). The modified TE, in the active state, either catalyses primer extension or is necessary for primer extension to occur. It can be reactivated by incubation in the amplification reaction mixt. at elevated temps.

ADVANTAGE - **Non-specific** amplification is greatly reduced as the reaction mixt. does not support primer extension until the temp. of the reaction mixt. has been elevated to a temp. which ensures primer hybridisation specificity. The heat inactivated enzymes are storage stable.

Dwg.0/5

FS CPI
FA AB
MC CPI: B04-L04A; D05-A02; D05-H18B
ABEQ US 5677152 A UPAB: 19971125
Method for the amplification of a target nucleic acid contained in a sample comprises: (a) contacting the sample with an amplification reaction mixture containing a primer complementary to the target nucleic acid and a modified thermostable enzyme, where the modified thermostable enzyme is produced by a reaction of a mixture of a thermostable polymerase and a modifier reagent, where the reaction is carried out at alkaline pH at a temperature which is < 25 deg. C., where the reagent is a dicarboxylic acid anhydride of general formula (I): where R1 and R2 = H or organic radicals, which may be linked, or of formula (II): where R1 and R2 are organic radicals, which may be linked, and the H are cis and where the reaction results in complete inactivation of enzyme activity; and (b) incubating the resulting mixture of step (a) at a temperature > 50 deg. C. to reactivate the enzyme and allow formation of primer extension products.

Dwg.0/5

L98 ANSWER 17 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1996-261625 [27] WPIX
DNN N1996-220038 DNC C1996-082910
TI Oligo nucleotide probes with intercalating fluoro chrome label - only fluoresces when **bound** to target sequences, removes need to separate un-hybridised probes.
DC B04 D16 S03
IN INOUE, T; ISHIGURO, T; OTSUKA, M; SUGIURA, Y; YAWATA, H
PA (TOYJ) TOSOH CORP
CYC 6
PI EP 714986 A1 19960605 (199627)* EN 32p C12Q001-68 <--
R: DE FR GB IT
JP 08211050 A 19960820 (199643) 17p G01N033-50
US 5814447 A 19980929 (199846) C12Q001-68 <--
JP 2001013147 A 20010119 (200107) 19p G01N033-566
EP 714986 B1 20010314 (200116) EN C12Q001-68 <--
R: DE FR GB IT
DE 69520330 E 20010419 (200129) C12Q001-68 <--
JP 3189000 B2 20010716 (200142) 18p G01N033-50

ADT EP 714986 A1 EP 1995-308660 19951201; JP 08211050 A JP 1995-185599 19950721; US 5814447 A US 1995-564650 19951129; JP 2001013147 A Div ex JP 1995-185599 19950721, JP 2000-154431 19950721; EP 714986 B1 EP 1995-308660 19951201; DE 69520330 E DE 1995-620330 19951201, EP 1995-308660 19951201; JP 3189000 B2 JP 1995-185599 19950721
FDT DE 69520330 E Based on EP 714986; JP 3189000 B2 Previous Publ. JP 08211050
PRAI JP 1995-185599 19950721; JP 1994-298665 19941201
REP EP 487218; EP 488243; EP 492570; EP 512334; FR 2686621
IC ICM **C12Q001-68**; G01N033-50; G01N033-566
ICS **C12N015-09**; **C12P019-34**; G01N021-78; G01N033-53; G01N033-533; G01N033-536; G01N033-58
ICA C07H021-04
AB EP 714986 A UPAB: 19960710
Single-stranded oligonucleotides (I) labelled with an intercalating fluorochrome are new.

USE - (I) are useful as probes in hybridisation assays (claimed) in which a single- or double-stranded nucleic acid having a target sequence complementary to the probe is contacted (opt. after amplification of at least the target sequence) with the probe so that the probe **binds** to the target sequence and the fluorochrome is intercalated into the **binding** region.

ADVANTAGE - Provided that the fluorescent characteristics of the fluorochrome change when the probe is hybridised to the target sequence, homogeneous assays can be performed without the need to separate unhybridised probe. If the probe is added before PCR amplification of the target sequence, the PCR time profile can be monitored by measuring the fluorescent intensity of the reaction mixt. during amplification, while avoiding the problem of **nonspecific** intercalation associated with the use of free fluorochromes (cf. J0237000/1993).

Dwg.0/21
FS CPI EPI
FA AB; DCN
MC CPI: B04-B03C; B04-E05; D05-H09; D05-H12D1; D05-H18
EPI: S03-E14H; S03-E14H4

L98 ANSWER 18 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1996-160381 [16] WPIX
DNC C1996-050700
TI Reducing **non-specific** hybridisation - by using non-natural nucleotide units in hybridisation assays, aptamers or anti sense molecules.
DC B04 D16
IN COLLINS, M L; HORN, T; SHERIDAN, P E; URDEA, M S; WARNER, B D; COLLINS, M; SHERIDAN, P; URDEA, M; WARNER, B; SHERIDAN, P J
PA (CHIR) CHIRON DIAGNOSTICS CORP; (CHIR) CHIRON CORP; (FARB) BAYER CORP; (COLL-I) COLLINS M L; (HORN-I) HORN T; (SHER-I) SHERIDAN P J; (URDE-I) URDEA M S; (WARN-I) WARNER B D
CYC 49
PI WO 9606950 A1 19960307 (199616)* EN 65p C12Q001-68 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KR KZ LT LV MX NO NZ PL RO RU SG SI SK TJ TM UA UZ
AU 9534631 A 19960322 (199626) C12Q001-68 <--
NO 9700884 A 19970428 (199727) C12Q001-68 <--
EP 778898 A1 19970618 (199729) EN C12Q001-68 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
FI 9700803 A 19970423 (199729) C12Q000-00
CZ 9700589 A3 19970716 (199735) C12Q001-68 <--
US 5681702 A 19971028 (199749) 28p C12Q001-68 <--
BR 9508674 A 19971118 (199802) C12Q001-68 <--
SK 9700254 A3 19971210 (199811) C12Q001-68 <--
MX 9701419 A1 19970501 (199823) C12Q001-68 <--
JP 10506270 W 19980623 (199835) 67p C12Q001-68 <--

US 5780610 A 19980714 (199835) C07H021-04
KR 97705644 A 19971009 (199841) C12Q001-68 <--
HU 77754 T 19980728 (199842) C12Q001-68 <--
AU 708194 B 19990729 (199941) C12Q001-68 <--
NZ 292451 A 19990929 (199945) C07H019-20
KR 218113 B1 19991001 (200108) C12Q001-68 <--
EP 1097939 A2 20010509 (200128) EN C07H019-16
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 6232462 B1 20010515 (200129) C07H021-00
US 2001026918 A1 20011004 (200161) C12Q001-68 <--
EP 778898 B1 20021113 (200282) EN C12Q001-68 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

ADT WO 9606950 A1 WO 1995-US11115 19950830; AU 9534631 A AU 1995-34631 19950830; NO 9700884 A WO 1995-US11115 19950830, NO 1997-884 19970227; EP 778898 A1 EP 1995-931051 19950830, WO 1995-US11115 19950830; FI 9700803 A WO 1995-US11115 19950830, FI 1997-803 19970226; CZ 9700589 A3 WO 1995-US11115 19950830, CZ 1997-589 19950830; US 5681702 A US 1994-298073 19940830; BR 9508674 A BR 1995-8674 19950830, WO 1995-US11115 19950830; SK 9700254 A3 WO 1995-US11115 19950830, SK 1997-254 19950830; MX 9701419 A1 MX 1997-1419 19970225; JP 10506270 W WO 1995-US11115 19950830, JP 1996-508975 19950830; US 5780610 A Cont of US 1994-298073 19940830, Cont of US 1995-435547 19950505, US 1997-794153 19970203; KR 97705644 A WO 1995-US11115 19950830, KR 1997-701318 19970228; HU 77754 T WO 1995-US11115 19950830, HU 1998-852 19950830; AU 708194 B AU 1995-34631 19950830; NZ 292451 A NZ 1995-292451 19950830, WO 1995-US11115 19950830; KR 218113 B1 WO 1995-US11115 19950830, KR 1997-701318 19970228; EP 1097939 A2 Div ex EP 1995-931051 19950830, EP 2001-100768 19950830; US 6232462 B1 Cont of US 1994-298073 19940830, Cont of US 1995-435547 19950505, Cont of US 1997-794153 19970203, US 1998-115566 19980714; US 2001026918 A1 Cont of US 1994-298073 19940830, Cont of US 1995-435547 19950505, Cont of US 1997-794153 19970203, Div ex US 1998-115566 19980714, US 2000-752213 20001228; EP 778898 B1 EP 1995-931051 19950830, WO 1995-US11115 19950830, Related to EP 2001-100768 19950830

FDT AU 9534631 A Based on WO 9606950; EP 778898 A1 Based on WO 9606950; CZ 9700589 A3 Based on WO 9606950; BR 9508674 A Based on WO 9606950; JP 10506270 W Based on WO 9606950; US 5780610 A Cont of US 5681702; KR 97705644 A Based on WO 9606950; HU 77754 T Based on WO 9606950; AU 708194 B Previous Publ. AU 9534631, Based on WO 9606950; NZ 292451 A Based on WO 9606950; EP 1097939 A2 Div ex EP 778898; US 6232462 B1 Cont of US 5681002, Cont of US 5780610; US 2001026918 A1 Cont of US 5681702, Cont of US 5780610, Div ex US 6232462; EP 778898 B1 Related to EP 1097939, Based on WO 9606950

PRAI US 1994-298073 19940830; US 1995-435547 19950505; US 1997-794153 19970203; US 1998-115566 19980714; US 2000-752213 20001228

REP DE 4140463; EP 225807; EP 70685; WO 9516055

IC ICM C07H019-16; C07H019-20; C07H021-00; C07H021-04; C12Q000-00; **C12Q001-68**
ICS A23J001-00; C07H019-04; C07H021-02; C07K001-00; C07K014-00; C07K016-00; C07K017-00; **C12N015-09**; **C12P019-24**; **C12P019-34**

AB WO 9606950 A UPAB: 19960422
In a nucleic acid (NA) hybridisation assay for detecting a NA analyte in a sample using assay components each of which comprises at least 1 hybridising oligonucleotide (ON) segment, the improvement comprises incorporating into at least 1 hybridising ON segment a 1st nucleotidic unit which will not effectively base pair with adenosine (A), thymidine (T), cytidine (C), guanosine (G) or uridine (U) under conditions in which A-T and G-C base pairs are formed. Pref. the 1st nucleotidic unit can form a base pair with a 2nd, complementary nucleotidic unit. Esp. the non-natural base pair is formed between isocytosine and isoguanosine. Also claimed are: an ON as above useful as an aptamer ; an antisense molecule (AM) contg. a segment as above; hybridisation assays and kits using these components; and methods of preparing isoguanosine cpds. useful as the

nucleotidic units.
USE - The assay methods reduce **nonspecific** hybridisation to reduce background noise and increase sensitivity and specificity in the detection and quantitation of analytes. The aptamers and AMs prepd. using the non-natural nucleotidic units can also have minimised **nonspecific** hybridisation when used, e.g. in therapy.
Dwg.0/3
FS CPI
FA AB; GI; DCN
MC CPI: B04-B03; B04-E01; B04-E05; B11-C08E5; B12-K04F; D05-H09; D05-H12D2
ABEQ US 5681702 A UPAB: 19971211
A nucleic acid hybridization assay for detecting a nucleic acid analyte in a sample using a plurality of assay components each of which comprises at least one hybridizing oligonucleotide segment not involved in hybridization to the analyte, comprises:
incorporating into at least one hybridizing oligonucleotide segment a first nucleotidic unit which will not effectively base pair with adenosine (A), thymidine (T), cytidine (C), guanosine (G) or uridine (U) under conditions in which A-T and G-C base pairs are formed.
Dwg.0/3

L98 ANSWER 19 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1996-021916 [03] WPIX
DNC C1996-007631
TI Determn. of concn. of target nucleic acid in a polymerase chain reaction - by thermal cycling a reaction mixt. contg. reporter molecules which make double stranded DNA measurable.
DC B04 D16
IN ATWOOD, J G
PA (PEKE) PERKIN-ELMER CORP
CYC 8
PI EP 686699 A2 19951213 (199603)* EN 28p C12Q001-68 <--
R: DE FR GB IT NL
CA 2151065 A 19951209 (199614) C12Q001-68 <--
JP 08066199 A 19960312 (199620) 19p C12Q001-68 <--
EP 686699 A3 19960417 (199626) C12Q001-68 <--
US 5766889 A 19980616 (199831) C07H021-04
ADT EP 686699 A2 EP 1995-108649 19950606; CA 2151065 A CA 1995-2151065 19950606; JP 08066199 A JP 1995-140865 19950607; EP 686699 A3 EP 1995-108649 19950606; US 5766889 A US 1994-255507 19940608
PRAI US 1994-255507 19940608
REP 5.Jnl.Ref; EP 640828
IC ICM C07H021-04; **C12Q001-68**
ICS C12M001-40; **C12N015-09**; **C12P019-34**; C12Q001-70; G01N033-58
AB EP 686699 A UPAB: 19960122
Starting molar concn. of target nucleic acid molecules at the beginning of a polymerase chain reaction in a sample reaction mixt. which contains suitable buffers, two complimentary kinds of oligonucleotide primers, a molar excess of four kinds of nucleotide triphosphates, a DNA polymerase, and the target nucleic acid, is determined by providing the two primers in known concn. and adding a reporter molecule which does not interfere with the reaction but makes the double stranded DNA (dsDNA) created by the reaction mixt. detectable. One or more standard reaction mixts. which are the same but have known starting concns. of target nucleic acid molecules are thermally cycled to obtain growth curves with known starting molar concns. of target DNA molecules, with the reaction mixt. excited during at least the extension portion of each cycle, measuring the intensity of the signal of the reporter molecule during each cycle, converting the signal to molar concn. dsDNA and generating a curve of molar concn. dsDNA versus cycle number. The measured curve is used, by successive approximations, to determine the constants to provide a best fit to the one or more known growth curves according to one or other of two stated relations, such that

the molar concn. of starting nucleic acid of the unknown sample can be evaluated by fixing the equation constants and varying the starting concn. to get a best fit to the measured growth curve of each unknown sample. Also claimed are methods and appts. using a microcomputer to evaluate the molar concn. values of dsDNA in the mixt. and control the procedure.

USE - The method is used in quantitative analysis of nucleic acid samples, such as DNA in a polymerase process.

ADVANTAGE - The appts. enables automated operation with real time monitoring of DNA during thermal cycling and prediction of molar concn. of starting copies of the target or template DNA even though the primer concn. has run to exhaustion, or the exponential amplification process may not have been continued to completion. It is only necessary for a significant number of cycles to be performed so that amplification above the level of **non-specific** background is achieved and the values of characteristic parameters determined.

Dwg.4/4

FS CPI
FA AB; GI
MC CPI: B04-B03B; B04-B03C; B04-E01; B04-L04A; B11-C07B; B12-K04F; D05-H09; D05-H18B

L98 ANSWER 20 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1995-383306 [50] WPIX
DNC C1995-165718
TI Amplifying target nucleic acid by strand displacement amplification - using thermophilic DNA polymerase and thermophilic restriction endonuclease.
DC B04 D16
IN FRAISER, M S; SPARGO, C A; VAN, CLEVE M; WALKER, G T; WRIGHT, D J; LITTLE, M C
PA (BECT) BECTON DICKINSON & CO; (BECT) BECTON DICKINSON CO
CYC 20

PI	AU 9514776	A	19951026 (199550)*	47p	C12Q001-68	<--
	EP 684315	A1	19951129 (199601) EN	27p	C12Q001-68	<--
	R: AT BE CH DE ES FR GB IT LI NL SE					
	JP 07289298	A	19951107 (199602)	19p	C12Q001-68	<--
	BR 9501581	A	19951114 (199603)		C12P019-34	<--
	CA 2144495	A	19951019 (199608)		C12N015-10	
	SG 28239	A1	19960401 (199633)		C12P000-00	
	US 5648211	A	19970715 (199734)	18p	C12Q001-68	<--
	US 5744311	A	19980428 (199824)	18p	C12Q001-68	<--
	AU 695574	B	19980813 (199844)		C12Q001-68	<--
	KR 156290	B1	19981015 (200027)		C12Q001-68	<--
	JP 3140937	B2	20010305 (200115)	19p	C12Q001-68	<--
	TW 408224	A	20001011 (200116)		C12Q001-68	<--
	CA 2144495	C	20011023 (200170) EN		C12N015-10	
	MX 198837	B	20000929 (200211)		C12P019-34	<--
	EP 684315	B1	20020626 (200242) EN		C12Q001-68	<--
	R: AT BE CH DE ES FR GB IT LI NL SE					
	DE 69527171	E	20020801 (200258)		C12Q001-68	<--
	ES 2174884	T3	20021116 (200302)		C12Q001-68	<--

ADT AU 9514776 A AU 1995-14776 19950313; EP 684315 A1 EP 1995-103569 19950313; JP 07289298 A JP 1995-88242 19950413; BR 9501581 A BR 1995-1581 19950413; CA 2144495 A CA 1995-2144495 19950313; SG 28239 A1 SG 1995-187 19950329; US 5648211 A US 1994-229279 19940418; US 5744311 A Cont of US 1994-229279 19940418, US 1996-701269 19960822; AU 695574 B AU 1995-14776 19950313; KR 156290 B1 KR 1995-9039 19950418; JP 3140937 B2 JP 1995-88242 19950413; TW 408224 A TW 1995-102392 19950314; CA 2144495 C CA 1995-2144495 19950313; MX 198837 B MX 1995-1353 19950314; EP 684315 B1 EP 1995-103569 19950313; DE 69527171 E DE 1995-627171 19950313, EP 1995-103569 19950313; ES 2174884 T3 EP 1995-103569 19950313
FDT AU 695574 B Previous Publ. AU 9514776; JP 3140937 B2 Previous Publ. JP 07289298; DE 69527171 E Based on EP 684315; ES 2174884 T3 Based on EP

684315
PRAI US 1994-229279 19940418; US 1996-701269 19960822
REP 01Jnl.Ref; EP 497272; WO 9201813; WO 9209689
IC ICM C12N015-10; C12P000-00; **C12P019-34**; **C12Q001-68**
ICS C07H021-00; C12N009-12; C12N009-16; **C12N015-09**; C12Q001-44; C12Q001-48; C12Q001-70; G01N033-58; G01N033-68
AB AU 9514776 A UPAB: 19951215
A novel method for amplifying a target sequence (TS) comprises: (1) **binding** to the 3' end of a single stranded nucleic acid (ssNA) fragment contg. a TS, a primer (P) for strand displacement amplification (SDA), so that P forms a 5'-single strand overhang, P contains a recognition/cleavage site for a thermophilic restriction endonuclease (TRE) that does not cut in the TS; (2) extending P in presence of: (a) a thermophilic DNA polymerase active at 50-70deg.C. having strand-displacement activity but no 5'-3' exonuclease activity; (b) dNTPs; (c) one deriv. dNTP; and (d) TRE (active at 50-70deg.C.) that nicks the recognition/cleavage site when this is hemimodified by incorporation of derivs. dNTP so as to produce an extension prod. (EP) consisting of a newly synthesised strand complementary to TS and double stranded hemimodified TRE site; (3) nicking the hemimodified site with TRE; (4) extending from the nick, using the polymerase, so as to displace the newly synthesised strand, genera ting a second extension prod. (EP2) comprising a second newly synthesised strand; and (5) repeating the nicking, extension and displacement steps so that the TS is amplified.

USE - Nucleic acid amplification is used in diagnosis of infectious and genetic diseases, isolation of genes and forensic medicine.

ADVANTAGE - The method can be done over a wider temp. range than conventional SDA (limited to 37-42deg.C.). Operation at high temp.: (1) improves specificity and efficiency; (2) reduces **non-specific** background amplification; (3) may increase yield of amplification prods.; (4) eliminates the need to add enzymes after initial heat denaturation; and (5) improves effect of uracil DNA glycosylase (UDG) decontamination of target specific amplicons.

Dwg.0/2
FS CPI
FA AB
MC CPI: B04-E01; B04-E05; B11-C08E5; B12-K04A; D05-H09; D05-H18B
ABEQ US 5648211 A UPAB: 19970820
A method for amplifying a target sequence comprising:

A) providing a single stranded nucleic acid fragment containing the target sequence, the fragment having a 5 end and a 3 end;

B) **binding** an amplification primer for SDA to the 3 end of the fragment such that the primer forms a 5 single stranded overhang, the amplification primer comprising a recognition/cleavage site for a thermophilic restriction endonuclease which does not cut the target nucleic acid sequence, and;

C) amplifying the target sequence at 50 deg. C.-60 deg. C. in a reaction comprising the steps of

i) extending the amplification primer on the fragment in the presence of

a) a thermophilic DNA polymerase having a temperature optimum for polymerizing activity of 65 deg. C.-75 deg. C., the polymerase having strand displacing activity and lacking 5'-3' exonuclease activity,

b) deoxynucleoside triphosphates,

c) at least one derivatised deoxynucleoside triphosphate, and

d) a thermophilic restriction endonuclease which nicks the recognition/cleavage site when the site is hemi-modified by incorporation of the derivatised deoxynucleoside triphosphate, the endonuclease having a temperature optimum for cleavage of double-stranded DNA of 50 deg. C.-65 deg. C.,

thereby producing a first double stranded product comprising the amplification primer, a first newly synthesized strand complementary to the target sequence, and a double stranded hemi-modified restriction

endonuclease recognition/cleavage site;
ii) nicking the double stranded hemi-modified restriction endonuclease recognition/cleavage site with the restriction endonuclease;
iii) extending from the nick using the DNA polymerase, thereby displacing the first newly synthesized strand from the fragment and generating a second extension product comprising a second newly synthesized strand, and;
iv) repeating the nicking, extending and displacing steps such that the target sequence is amplified.
Dwg.0/2

L98 ANSWER 21 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1995-329633 [43] WPIX
DNN N1995-248078 DNC C1995-146194
TI Device for manipulation of nucleic acids, esp. amplification and detection processes - comprising reaction cell defined by a transparent sample carrier surrounded by an open ended cylinder.
DC B04 D16 S03
IN KANDOLF, R
PA (BOEF) BOEHRINGER MANNHEIM GMBH; (HOFF) ROCHE DIAGNOSTICS GMBH
CYC 13
PI EP 673679 A1 19950927 (199543)* DE 14p B01L003-00
R: AT BE CH DE ES FR GB IT LI NL
DE 4409705 A1 19950928 (199544) 10p C07H021-00
AU 9514991 A 19950928 (199546) C12M001-00
JP 07289233 A 19951107 (199602) 11p C12M001-00
CA 2145029 A 19950923 (199603) C12Q001-68 <--
ADT EP 673679 A1 EP 1995-103907 19950317; DE 4409705 A1 DE 1994-4409705 19940322; AU 9514991 A AU 1995-14991 19950321; JP 07289233 A JP 1995-90150 19950322; CA 2145029 A CA 1995-2145029 19950320
PRAI DE 1994-4409705 19940322
REP 1.Jnl.Ref; GB 2177200; WO 9319207
IC ICM B01L003-00; C07H021-00; C12M001-00; **C12Q001-68**
ICS B01L007-00; C12M001-14; C12M001-40; **C12N015-09**; **C12P019-34**; G01N001-30
ICA C12Q001-70
AB EP 673679 A UPAB: 19990416
Device for manipulating nucleic acids (I) in a sample comprises a carrier (1) contg. at least 1 flat, transparent region (2) of sufficient size to take a sample, and at least 1 component (10) having a hole (11) and upper (12) and lower (13) inside dia..
Also new is a device comprising a plate with >1 carrier (1) and a flat component with >1 hole corresp. to the shape of the transparent regions (2).
USE - The device is used to amplify (I) on the carrier (pref. in the presence of labelled nucleotides) and then to opt. detect the amplification prods. (claimed). It can be used with cells, cytospins or chromosomal prepns., but partic. with tissue sections for the detection of pathogen-related (I).
ADVANTAGE - The device improves efficiency and sensitivity (the amplification rate may be 1000 x greater than with usual methods), suppresses **non-specific** reactions and is suitable for automation. It removes the need for using mineral oil to prevent evapn. and, where a large number of (I) are present on a carrier plate, many analyses can be performed simultaneously.
Dwg.1/7
FS CPI EPI
FA AB; GI
MC CPI: B04-E02; B11-C08E4; B11-C08E5; B12-K04F; D05-A02B; D05-A02C; D05-H09; D05-H18B
EPI: S03-E13D; S03-E14H

L98 ANSWER 22 OF 32 WPIX (C) 2003 THOMSON DERWENT

AN 1995-215277 [28] WPIX
DNC C1995-099595
TI Amplification of poly nucleotide(s) using thermostable enzymes - derived from Thermus thermophilus, allows reduction in **non-specific** hybridisation and high specificity..
DC B04 D16
IN INOUE, H; KAWAMURA, Y; SHIBATA, S; TAKARADA, Y
PA (TOYM) TOYO BOSEKI KK; (TOYM) TOYOBO KK
CYC 18
PI WO 9515399 A1 19950608 (199528)* EN 59p C12Q001-68 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: US
JP 07203999 A 19950808 (199540) 19p C12Q001-68 <--
EP 682121 A1 19951115 (199550) EN 33p C12Q001-68 <--
R: BE DE FR GB NL
US 5981183 A 19991109 (199954) C12Q001-68 <--
US 6303306 B1 20011016 (200164) C12Q001-68 <--
JP 3241555 B2 20011225 (200203) 17p C12Q001-68 <--
JP 2001299375 A 20011030 (200204) 20p C12N015-09 <--
EP 682121 B1 20020828 (200264) EN C12Q001-68 <--
R: BE DE FR GB NL
DE 69431240 E 20021002 (200273) C12Q001-68 <--
EP 1251182 A2 20021023 (200277) EN C12Q001-68 <--
R: BE DE FR GB NL
ADT WO 9515399 A1 WO 1994-JP2025 19941201; JP 07203999 A JP 1994-294980 19941129; EP 682121 A1 WO 1994-JP2025 19941201, EP 1995-902289 19941201; US 5981183 A Cont of WO 1994-JP2025 19941201, Cont of US 1995-446709 19950530, US 1997-821782 19970320; US 6303306 B1 Cont of WO 1994-JP2025 19941201, Cont of US 1995-446709 19950530, Cont of US 1997-821782 19970320, US 1999-292435 19990415; JP 3241555 B2 JP 1994-294980 19941129; JP 2001299375 A Div ex JP 1994-294980 19941129, JP 2001-103698 19941129; EP 682121 B1 WO 1994-JP2025 19941201, EP 1995-902289 19941201, Related to EP 2002-4130 19941201; DE 69431240 E DE 1994-631240 19941201, WO 1994-JP2025 19941201, EP 1995-902289 19941201; EP 1251182 A2 Div ex EP 1995-902289 19941201, EP 2002-4130 19941201
FDT EP 682121 A1 Based on WO 9515399; US 6303306 B1 Cont of US 5981183; JP 3241555 B2 Previous Publ. JP 07203999; EP 682121 B1 Based on WO 9515399; DE 69431240 E Based on EP 682121, Based on WO 9515399; EP 1251182 A2 Div ex EP 682121
PRAI JP 1993-301823 19931201
REP 01Jnl.Ref; EP 200362; EP 506889; EP 572417; JP 04067960; JP 0505105; JP 06502767; US 4683195; US 5322770; WO 9109944; WO 9208800
IC ICM **C12N015-09; C12Q001-68**
ICS C07H021-04; **C12P019-34**
AB WO 9515399 A UPAB: 20011129
Amplification of specific nucleic acid sequences using thermostable enzymes, comprises: (1) hybridising a first primer (primer 1) to the 5'-end of target RNA (first template RNA) and extension using a thermostable RNA-dependent DNA polymerase; (2) removing the RNA strand from the RNA/DNA hybrid using a thermostable ribonuclease H, to give a single-stranded DNA; (3) hybridising a second primer (primer 2) to the 3'-end of the DNA strand, and extension using a thermostable DNA-dependent DNA polymerase to give a double-stranded DNA; (4) using a thermostable DNA-dependent RNA polymerase to generate single-stranded RNA from this double-stranded DNA; (5) hybridising primer 2 to the RNA produced from (4), and using the RNA as a template, extending the primer using a thermostable RNA dependent DNA polymerase to give a RNA/DNA hybrid; (6) removing the RNA strand using a thermostable ribonuclease H to obtain single-stranded DNA; (7) hybridising primer 1 to the DNA produced in (6), and using the DNA as a template, extending the primer using a thermostable DNA-dependent DNA polymerase to produce a double-stranded DNA; (8) generating a single-stranded RNA from the double-stranded DNA using a thermostable DNA-dependent RNA polymerase. This RNA is returned to step

(5) and the cycle repeated until the required amplification is achieved. A target DNA can be amplified by the same route: in this case step (1) is hybridisation of primer 1 at the 5'-end, and extension using a thermostable DNA-dependent DNA polymerase; step (2) is separation of the two DNA strands, steps (3) onwards are as above.

USE - The method is used for the effective amplification of target nucleic acid sequences.

ADVANTAGE - The amplification is achieved with high specificity and reduction in **non-specific** hybridisation, and without the need for sequential addition of enzymes.

Dwg.1/5

FS CPI
FA AB; GI
MC CPI: B04-E02; B04-E05; B04-L04A; D05-H18B

L98 ANSWER 23 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1994-341888 [42] WPIX
DNC C1994-155811
TI Method for the amplification of double stranded nucleic acid macromolecules - using inverse linkage oligo nucleotide(s) to reduce **non-specific** hybridisation.(Eng)..
DC B04 D16
IN COASSIN, P J; COOK, R M; KONRAD, K D; RAMPAL, J B
PA (BECI) BECKMAN INSTR INC
CYC 3

PI	WO 9424312	A2	19941027 (199442)*		95p	C12Q001-68	<--
	AU 9467077	A	19941108 (199507)			C12Q001-68	<--
	US 5462854	A	19951031 (199549)		39p	C12Q001-68	<--
	WO 9424312	A3	19941208 (199610)			C12Q001-68	<--
	EP 700449	A1	19960313 (199615)	EN		C12Q001-68	<--
	JP 08509129	W	19961001 (199705)		82p	C12Q001-68	<--

ADT WO 9424312 A2 WO 1994-US4275 19940419; AU 9467077 A AU 1994-67077 19940419; US 5462854 A US 1993-50681 19930419; WO 9424312 A3 WO 1994-US4275 19940419; EP 700449 A1 EP 1994-914832 19940419, WO 1994-US4275 19940419; JP 08509129 W JP 1994-523534 19940419, WO 1994-US4275 19940419
FDT AU 9467077 A Based on WO 9424312; EP 700449 A1 Based on WO 9424312; JP 08509129 W Based on WO 9424312
PRAI US 1993-50681 19930419
REP 4.Jnl.Ref
IC ICM **C12Q001-68**
ICS C07H021-00; C07H021-04; **C12N015-09**; **C12P019-34**
AB WO 9424312 A UPAB: 19941212

A process for the amplification of a double stranded nucleic acid macromolecule comprising a strand and a complementary strand is claimed, comprising: (a) separating the strand from the complementary strand, (b) treating the two strands obtained with at least one 3'-inverse linkage oligonucleotide(s) (ILO) where the sequence of each ILO is the same and comprises a first sequence complementary to one strand and a second sequence complementary to the other strand but which are not complementary to each other, under conditions which allow hybridisation so that both ILO sequences are extended to form ILO products; and (c) separating ILO products from the strand and repeating step (b) at least once so that at least one ILO product has a first 3' termini complementary to a second 3' termini, the first being hybridised to the second.

ADVANTAGE - The use of ILO's in nucleic acid amplification and analysis allows the amplification of nucleic acids without the problems encountered with other amplification techniques such as **non specific** hybridisation and amplification in the polymerase chain reaction (PCR) which results in noise. Whereas the ligation chain reaction, by definition, requires the use of four primers for amplification, the use of ILO's means that, if necessary, only one primer need be used.

Dwg.0/0

FS CPI
FA AB
MC CPI: B04-B03C; B04-E01; B11-C08E5; B12-K04F; D05-H10; D05-H12D1; D05-H18B
ABEQ US 5462854 A UPAB: 19951211
Amplification of double stranded nucleic acid with a single strand and a complementary strand comprises sepn. of the strand and its complement; incubation of both the strand and the complement with one or more (pref. labelled) oligonucleotides having inverse 3'-links and regions that are complementary to the single strand and to the complement, but not to each other, under conditions that favour hybridisation; extending the hybridisation with a suitable polymerase; sepn. of the single stranded prods. to obtain at least one prod. with complimentary 3'-termini, followed by hybridisation with the inverse 3'-linked oligonucleotide to form prods. with a partially double stranded circle; and further chain extension with a suitable polymerase.
USE - The process facilitates the identification of specific nucleic acid sequences.
ADVANTAGE - Amplification is facilitated by hybridisation and chain lengthening at two or more termini.
Dwg.0/6

L98 ANSWER 24 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1994-120177 [15] WPIX
DNC C1994-055582
TI Thermostable DNA polymerase compsn. - comprises temperature-sensitive polymerase inhibitor, for eliminating **non-specific** prod. formation in PCR.
DC B04 D16
IN CHRISTY, K G; DAISS, J L; ESDERS, T W; SCALICE, E R; SHARKEY, D J
PA (CLIN-N) CLINICAL DIAGNOSTIC SYSTEMS INC; (EAST) EASTMAN KODAK CO; (JOHJ) JOHNSON & JOHNSON CLINICAL DIAGNOSTICS INC; (JOHJ) JOHNSON & JOHNSON CLINICAL DIAGNOSTICS
CYC 13
PI EP 592035 A2 19940413 (199415)* EN 27p C12N015-10
R: AT BE CH DE FR GB IE IT LI NL SE
US 5338671 A 19940816 (199432) 17p C12P019-34 <--
JP 06209775 A 19940802 (199435) 20p C12N009-98
EP 592035 A3 19940914 (199532) C12N015-10
EP 592035 B1 19960103 (199606) EN 27p C12N015-10
R: AT BE CH DE FR GB IE IT LI NL SE
DE 69301221 E 19960215 (199612) C12N015-10
US 5587287 A 19961224 (199706) 17p C12Q001-68 <--
JP 2647794 B2 19970827 (199739) 20p C12N015-09 <--
ADT EP 592035 A2 EP 1993-202801 19931001; US 5338671 A US 1992-958144 19921007; JP 06209775 A JP 1993-274812 19931007; EP 592035 B1 EP 1993-202801 19931001; DE 69301221 E DE 1993-601221 19931001, EP 1993-202801 19931001; US 5587287 A Div ex US 1992-958144 19921007, US 1994-224218 19940407; JP 2647794 B2 JP 1993-274812 19931007
FDT DE 69301221 E Based on EP 592035; US 5587287 A Div ex US 5338671; JP 2647794 B2 Previous Publ. JP 06209775
PRAI US 1992-958144 19921007; US 1994-224218 19940407
REP No-SR.Pub; 1.Jnl.Ref; EP 415755; GB 2230011; WO 8906691; WO 9112342; 01Jnl.Ref
IC ICM C12N009-98; **C12N015-09**; C12N015-10; **C12P019-34**; **C12Q001-68**
ICS C07K015-28; C07K016-10; C07K016-40; C12N015-06; C12P021-08; C12Q001-70; G01N033-53
ICI C12P021-08, C12R001:91; C12P021-08, C12R001:
AB EP 592035 A UPAB: 19951109
A compsn. comprising a thermostable DNA polymerase and a temp.-sensitive inhibitor for the polymerase, is new. The inhibitor can inhibit DNA polymerase at temp. T1, which is less than 85 deg.C., such that enzymatic activity is inhibited and it is irreversibly inactivated at temp. T2,

which is above T1 and less than 40 deg.C., hence the polymerase regains activity.

Also claimed is (1) a method for amplifying a target nucleic acid (NA), comprising: (a) contacting a specimen suspected of contg. the NA with the following PCR reagents: (i) a primer, complementary to the NA; (ii) a thermostable DNA polymerase; (iii) a temp.-sensitive inhibitor of the polymerase; (iv) a DNA polymerase co-factor; (v) at least 2 deoxyribonucleoside-5-triphosphates; and (b) bringing the resultant mix to at least T2 to inactivate the polymerase inhibitor to allow formation of extension prods.; and (2) a monoclonal antibody (MAb), specific for thermostable DNA polymerase, with (a) an association constant of at least 1x10power7 molar-1, with the polymerase; (b) inhibit the polymerase at T1; and inactivated at T2 ; and (c) is Igm or Igc.

USE - The Ab inhibitors are useful for reducing or eliminating the formation of **non-specific** prods. in PCR methods.

Dwg.0/1

Dwg.0/1

FS CPI

FA AB

MC CPI: B04-B03C; B04-E01; B04-E05; B04-G03; B04-G21; B04-L02; B04-L04A; B04-M01; B11-C08E5; B12-K04F; B14-D06A; D05-H11A; D05-H18B

ABEQ US 5338671 A UPAB: 19940928

Amplification of target nucleic acid comprises contacting a sample with PCR reagents and heating to over 40 deg. C to inactivate thermostable DNA polymerase inhibitor and to allow formation of primer extension prods.. Reagents include a primer, thermostable DNA polymerase, temp.-sensitive inhibitor for the polymerase, a DNA polymerase cofactor and more than deoxyribonucleoside-5'-triphosphate.

USE - Used in a diagnostic rest kit suitable for PCR.

Dwg.0/1

ABEQ EP 592035 B UPAB: 19960212

A composition comprising a thermostable DNA polymerase, the composition characterized wherein it further comprises a temperature sensitive inhibitor for the DNA polymerase, the inhibitor being capable of inhibiting the DNA polymerase at a temperature T1 which is less than 85deg.C such that enzymatic activity of the DNA polymerase is inhibited, and the inhibitor being irreversibly inactivated at a temperature T2 which is greater than T1 and is also greater than 40deg.C, so that the DNA polymerase regains its enzymatic activity.

Dwg.0/1

ABEQ US 5587287 A UPAB: 19970205

A new composition comprises: a thermostable DNA polymerase, and a temperature sensitive inhibitor for said DNA polymerase,

said inhibitor being an antibody which is specific to said thermostable DNA polymerase and which inhibits said thermostable DNA polymerase at a temperature T1 which is less than about 85deg. C. such that enzymatic activity of said thermostable DNA polymerase is inhibited, and

said inhibitor being irreversibly inactivated at a temperature T2 which is greater than T1 and is also greater than about 40 deg. C., so that said thermostable DNA polymerase regains its enzymatic activity,

wherein said thermostable DNA polymerase is stable at T2.

Dwg.0/1

L98 ANSWER 25 OF 32 WPIX (C) 2003 THOMSON DERWENT

AN 1993-284688 [36] WPIX

CR 1993-199728 [25]

DNC C1993-126752

TI Amplification and detection of specific nucleic acid sequence - using oligo nucleotide(s) with sequences complementary and homologous to sequence of interest.

DC B04 D16 J04

IN AONO, T; SHIBATA, S; TAKARADA, Y

PA (TOYM) TOYOBO KK; (TOYM) TOYO BOSEKI KK
CYC 2
PI JP 05199900 A 19930810 (199336)* 12p C12Q001-68 <--
US 5525462 A 19960611 (199629) 20p C12Q001-68 <--
JP 3109033 B2 20001113 (200060) 12p C12Q001-68 <--
ADT JP 05199900 A JP 1992-110959 19920430; US 5525462 A US 1992-875758 19920428; JP 3109033 B2 JP 1992-110959 19920430
FDT JP 3109033 B2 Previous Publ. JP 05199900
PRAI JP 1991-130360 19910502; JP 1991-315483 19911101
IC ICM **C12Q001-68**
ICS C07H021-00; C07H021-04; **C12N015-09**; C12N015-10; **C12P019-34**
AB JP 05199900 A UPAB: 20001123
An oligonucleotide (II) contains base sequences A and B (where from 5'-terminal to 3'-terminal, the base sequence B is complementary to a part of a specific nucleic acid (NA) sequence and the base sequence A is homologous to the 3'-downstream sequence of a part of the specific NA sequence in order.

NA sequence is amplified by amplifying at least one specific NA sequence in a sample as follows: (a) a first oligonucleotide (I) complementary to a part of the specific NA sequence, and the second oligonucleotide (II) are mixed with the sample and reacted to anneal (I) and (II) to the specific NA sequence in the sample; (b) the oligonucleotide from (I) obtd. in (a) is used as a primer to extend the nucleotide to the 5'-terminal of the second oligonucleotide of the annealing substance, (c) 3'-terminal of the extended polynucleotide from (b) is ligated to 5'-terminal of the second annealed oligonucleotide, (d) the ligated prod. is sepd. from the synthesised template to produce a single stranded molecule; (e) the single stranded molecule formed by (a) is used as a template, and the first oligonucleotide is used as a primer to synthesise extended prod. of nucleotide.

A reagent kit for detecting a target NA contains labelled first and/or second oligonucleotide, ligation enzyme, NA polymerase and/or reverse transcriptase, 4 kinds of deoxynucleotide 3 phosphates, reaction buffer and the label detecting system.

USE/ADVANTAGE - **Non-specific** reaction is inhibited, and specific sequence only can be amplified

Dwg.0/5
Dwg.0/5
FS CPI
FA AB
MC CPI: B04-B02C; B04-B04A1; B12-K04; D05-H09; J04-B01
ABEQ US 5525462 A UPAB: 19960724
A method for amplifying at least one specific nucleic acid sequence contained in a sample, using initially as a primer an oligonucleotide having at least a base sequence A, which is 10-30 nucleotides in length and homologous to a part of a specific nucleic acid sequence to be amplified, and a base sequence B, which is 10-30 nucleotides in length and complementary to a sequence 3' to the part of the specific nucleic acid sequence to be amplified, wherein sequence A and sequence B are separated by a spacer region of 0-20 nucleotides and sequence A is located at the 5' end of the oligonucleotide and sequence B is located at the 3' end of the oligonucleotide, which comprises the following procedures:

(a) annealing sequence B of said oligonucleotide to the sequence 3' to the part of the specific nucleic acid sequence to be amplified in the sample to provide a first primer;

(b) elongating sequence B of the oligonucleotide, which was annealed to the sequence 3' to the part of the specific nucleic acid sequence to be amplified in the sample in (a);

(c) digesting from the 3' end of the oligonucleotide, which did not anneal to the specific nucleic acid sequence to be amplified in the sample in (a), with an exonuclease III, except for at least a part of the base sequence A, which will function as a second primer in (e);

(d) denaturing the elongation product obtained in (b) to a single strand; and

(e) annealing sequence A of the oligonucleotide of (c) as a second primer to the single strand in (d), and elongating the sequence A of the oligonucleotide of (c) using the single strand obtained in (d) as a template.

Dwg.0/10

L98 ANSWER 26 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1993-199728 [25] WPIX
CR 1993-284688 [36]
DNC C1993-088371
TI Amplification of nucleotide sequence - using two nucleotide complementary sequences, annealing, degrading unreacted material, denaturing etc..
DC B04 D16 J04
IN AONO, T; SHIBATA, S; TAKARADA, Y
PA (TOYM) TOYOBO KK; (TOYM) TOYO BOSEKI KK
CYC 2
PI JP 05123171 A 19930521 (199325)* 8p C12N015-10
US 5525462 A 19960611 (199629) 20p C12Q001-68 <--
JP 3275969 B2 20020422 (200234) 9p C12N015-09 <--
ADT JP 05123171 A JP 1991-315483 19911101; US 5525462 A US 1992-875758 19920428; JP 3275969 B2 JP 1991-315483 19911101
FDT JP 3275969 B2 Previous Publ. JP 05123171
PRAI JP 1991-315483 19911101; JP 1991-130360 19910502
IC ICM **C12N015-09**; C12N015-10; **C12Q001-68**
ICS C07H021-04; **C12P019-34**
AB JP 05123171 A UPAB: 20020528
In the method, (a) oligonucleotides containing the nucleotide sequence A which is complementary to the part of the specific nucleotide sequence (5' to 3') and the nucleotide sequence B which is complementary to the 3' down steam of the specific nucleotide sequence, and the sample are reacted. The specific nucleotide sequence in the sample and the oligonucleotide are annealed. (b) The prolonged reaction is carried out using the annealed oligonucleotides as primer. (c) Part of the nucleotide sequence A remain in the non-reacted oligonucleotide, and the rest is degradated. (d) The single stranded molecule is produced by the denaturation of the product (b). (e) The prolonged products are synthesised using the single stranded molecule (d) as template and oligonucleotides (c) as primer.

Pref. (f) the single stranded molecules are produced by the denaturation of the prolonged product (e); the prolonged product is synthesised using the oligonucleotides as primer and this step is repeated at least 1 time; or (f') the prolonged product (e) is treated by steps of (a)-(e) at least 1 time, and opt. (g) the amplified products (f) are treated of the steps (a)-(e) or (a)-(f) at least 1 time. The oligonucleotides in (f) or (g) may be different from the oligonucleotides using (a).

USE/ADVANTAGE - **Nonspecific** reaction is repressed and the amplification of the specific nucleotide sequence is possible

Dwg.0/0
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-B04A1; D05-H09; D05-H12
ABEQ US 5525462 A UPAB: 19960724
A method for amplifying at least one specific nucleic acid sequence contained in a sample, using initially as a primer an oligonucleotide having at least a base sequence A, which is 10-30 nucleotides in length and homologous to a part of a specific nucleic acid sequence to be amplified, and a base sequence B, which is 10-30 nucleotides in length and complementary to a sequence 3' to the part of the specific nucleic acid sequence to be amplified, wherein sequence A and sequence B are separated by a spacer region of 0-20 nucleotides and sequence A is located at the 5'

end of the oligonucleotide and sequence B is located at the 3' end of the oligonucleotide, which comprises the following procedures:

(a) annealing sequence B of said oligonucleotide to the sequence 3' to the part of the specific nucleic acid sequence to be amplified in the sample to provide a first primer;

(b) elongating sequence B of the oligonucleotide, which was annealed to the sequence 3' to the part of the specific nucleic acid sequence to be amplified in the sample in (a);

(c) digesting from the 3' end of the oligonucleotide, which did not anneal to the specific nucleic acid sequence to be amplified in the sample in (a), with an exonuclease III, except for at least a part of the base sequence A, which will function as a second primer in (e);

(d) denaturing the elongation product obtained in (b) to a single strand; and

(e) annealing sequence A of the oligonucleotide of (c) as a second primer to the single strand in (d), and elongating the sequence A of the oligonucleotide of (c) using the single strand obtained in (d) as a template.

Dwg.0/10

L98 ANSWER 27 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1991-267153 [36] WPIX
DNC C1991-115861
TI Improvements in specificity of polymerase chain reaction - involving changes in way polymerase chain reaction reagents are made by replacing mineral oil vapour barrier by grease or wax.
DC A89 B04 D16
IN BLOCH, W; RAYMOND, J; READ, A R; RAYMOND, J C; READ, A B
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (CETU) CETUS CORP; (HOFF) HOFFMANN LA ROCHE INC
CYC 18
PI WO 9112342 A 19910822 (199136)*
RW: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
W: AU CA JP US
AU 9173073 A 19910903 (199148)
EP 515506 A1 19921202 (199249) EN 47p C12Q001-68 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
JP 05506143 W 19930916 (199342) 15p C12M001-00
AU 653712 B 19941013 (199442) C12Q001-68 <--
US 5411876 A 19950502 (199523) 17p C12P019-34 <--
US 5565339 A 19961015 (199647) 17p C12P019-34 <--
CA 2075050 C 19981006 (199850) C12M001-24
EP 515506 B1 20000105 (200006) EN C12Q001-68 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69131891 E 20000210 (200015) C12Q001-68 <--
ES 2141088 T3 20000316 (200021) C12Q001-68 <--
JP 3087907 B2 20000918 (200048) 19p C12M001-00
JP 2000316561 A 20001121 (200064) 21p C12M001-00
ADT EP 515506 A1 EP 1991-904707 19910215, WO 1991-US1039 19910215; JP 05506143 W JP 1991-504571 19910215, WO 1991-US1039 19910215; AU 653712 B AU 1991-73073 19910215; US 5411876 A Cont of US 1990-481501 19900216, US 1992-890300 19920527; US 5565339 A Cont of WO 1991-US1039 19910215, Cont of US 1992-920431 19921008, US 1994-325134 19941020; CA 2075050 C CA 1991-2075050 19910215; EP 515506 B1 EP 1991-904707 19910215, WO 1991-US1039 19910215; DE 69131891 E DE 1991-631891 19910215, EP 1991-904707 19910215, WO 1991-US1039 19910215; ES 2141088 T3 EP 1991-904707 19910215; JP 3087907 B2 JP 1991-504571 19910215, WO 1991-US1039 19910215; JP 2000316561 A Div ex JP 1991-504571 19910215, JP 2000-115806 19910215
FDT EP 515506 A1 Based on WO 9112342; JP 05506143 W Based on WO 9112342; AU 653712 B Previous Publ. AU 9173073, Based on WO 9112342; EP 515506 B1 Based on WO 9112342; DE 69131891 E Based on EP 515506, Based on WO 9112342; ES 2141088 T3 Based on EP 515506; JP 3087907 B2 Previous Publ. JP

05506143, Based on WO 9112342
PRAI US 1990-481501 19900216; US 1992-890300 19920527
REP DE 100617; EP 258017; EP 381501; US 4889818; WO 8806634
IC ICM C12M001-00; C12M001-24; **C12P019-34; C12Q001-68**
ICS B01J008-06; B01L003-14; B29C059-10; C08J007-04; C08L091-06; **C12N015-09**
AB WO 9112342 A UPAB: 19930928
A polymerase chain reaction (PCR) tube comprising a container and an aq. mixt. comprising all PCR reagents except a magnesium cpd., the total magnesium concn. in the mixt. being less than 10 power (-4) M, is claimed. Pref. the container contains two complementary subsets of PCR reagents in aq. mixts. sepd. by a layer of grease or wax. The aq. mixt. of PCR reagents is pref. sepd. from the atmos. above by a mass of grease or wax sufficient to completely effect sepn. Also claimed are a compsn. consisting of a mass of grease or wax in the range of 5-50mg contained within a container for holding 10-200 micro-l vol. of PCR reagents and test sample; and a kit contg. the improved containers. The prefd. compsn. consists of wax mixed with a nonionic surfactant, and melts at 40-90 deg.C. The surfactant is dissolved in the wax to a concn. of 0.1-10%. Prefd. are Tween 65 and Tween 85 (both RTM). Also claimed is a PCR reaction tube comprising (1) a container, (2) an aq. mixt. of PCR reagents, test sample and PCR prod., (3) a liq. barrier of wax or grease completely covering the aq. mixt., and (4) a second aq. mixt. above the layer of wax or grease, the second mixt. comprising a reagent for reacting with the PCR prod., e.g. an isopsoralen.

USE/ADVANTAGE - The novel change in the way that PCR reagents are mixed and the enzymatic reaction is started, and the replacement of mineral oil, commonly used as a vapour barrier to minimise solvent evapn., by a grease or wax, result in improvements to the PCR process for in vitro enzymatic amplification. of specific nucleic acid sequences. The use of the sepd. mixts. allows for the delay of reagent mixing until the first heating step of a PCR amplificn., thereby reducing the enzymatic generation of **nonspecific** prods. which occurs when a complete mixt. of PCR reagents, with or without test sample, stands at room temp. or below. The mixts. also increase the shelf-life of PCR reagents and increase protection of the laboratory environment a
FS CPI
FA AB; DCN
MC CPI: A12-W11L; B04-B01C; B04-C03; B10-J02; B11-C06; D05-C07; D05-H09; D05-H12
ABEQ JP 05506143 W UPAB: 19931202
Polymerase chain reaction (PCR) tube comprises a container and an aq. mixt. comprising all PCR reagents except a Mg cpd., the total Mg concn. in the mixt. being less than 10 power (-4) M.

Pref. the container contains two complementary subsets of PCR reagents in aq. mixts. sepd. by a layer of grease or wax. Aq. mixt. of PCR reagents is pref. sepd. from the atmos. above by a mass of grease or wax to completely effect sepn. Compsn. consists of a mass of grease or wax in the range of 5-50 mg contained within a container for holding 10-200 micro-1 vol. of PCR reagents and test sample; and a kit contg. the improved containers. Pref. compsn. consists of wax mixed with a nonionic surfactant, and melts at 40-90 deg.C. Surfactant is dissolved in the wax to a concn. of 0.1-10%. Pref. are Tween 65 and Tween 85 (both RTM). Also described is a PCR reaction tube comprising (1) a container, (2) an aq. mixt. of PCR agents, test sample and PCR prod., (3) a liq. barrier of wax or grease completely covering the aq. mixt., and (4) a second aq. mixt. above the layer of wax os grease, the second mixt. comprising a reagent for reacting with the PCR prod., e.g. an isopsoralen.

USE/ADVANTAGE - The change in the way that PCR reagents are mixed and the enzymatic reaction is started, and the replacement of mineral oil, commonly used as a vapour barrier to minimise solvent evapn., by a grease or wax, result in improvements to the PCR process for in vitro enzymatic amplification, of specific nucleic acid sequences. Sepd. mixts. allow for

the delay of reagent mixing until the first heating step of a PCR amplificn. reducing the enzymatic generation of **nonspecific** prods. which occurs when a complete mixt. of PCR reagents, with or without test sample, stands at room temp. or below. Mixts. also increase the shell-life of PCR reagents and increase protection of the laboratory environment against contamination by PCR prod.

ABEQ US 5411876 A UPAB: 19950619
PCR reaction tube comprises a container, an aq mixt of PCR reagents and grease or wax sufficient to completely separate the mixt from the above atmosphere when liquefied. Mixt has contact with the atmosphere.

The container is pref plastic and its inner surface is hydrophilic.

Also claimed are a compsn contg the container, a kit comprising the container, a method for sealing a PCR reaction tube and a method for producing a vapour barrier over PCR reagents in a tube.

USE/ADVANTAGE - For amplifying nucleic acids. Increased shelf-life and protection against the laboratory.
Dwg.0/0

ABEQ US 5565339 A UPAB: 19961124
A sealed container containing an aqueous solution comprising a thermostable DNA polymerase and a polymerase chain reaction (PCR) primer pair said pair flanking a predetermined nucleic acid sequence to be amplified by PCR wherein the magnesium concentration of the solution is less than about 10-4M.
Dwg.0/0

L98 ANSWER 28 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1990-209566 [27] WPIX
CR 1990-209563 [27]; 1990-209564 [27]; 1990-209565 [27]
DNC C1990-090511
TI Novel nucleic acid probes - are mono-disperse, super-paramagnetic particles useful in nucleic acid hybridisation assays and for sequencing oligo-nucleotide(s).
DC B04 D16 J04
IN HORNES, E; KORSNES, L
PA (DYNA-N) DYNAL AS; (HORN-I) HORNES E; (HOLM-I) HOLMES M J; (HORN-I) HORNES E
CYC 17
PI WO 9006045 A 19900614 (199027)* EN 45p
RW: AT BE CH DE ES FR GB IT LU NL SE
W: AU CH GB JP NO US
CA 2003508 A 19900521 (199031)
AU 9047586 A 19900626 (199038)
EP 446260 A 19910918 (199138) 45p
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04501959 W 19920409 (199221) 18p C12N015-11
AU 640626 B 19930902 (199342) C12Q001-68 <--
EP 446260 B1 19940302 (199409) EN 24p C12Q001-68 <--
R: AT BE CH DE ES FR GB IT LI LU NL SE
DE 68913555 E 19940407 (199415) C12Q001-68 <--
US 5512439 A 19960430 (199623) 17p C12P019-34 <--
JP 3020271 B2 20000315 (200018) 17p C12Q001-68 <--
CA 2003508 C 20000125 (200025) EN C12Q001-68 <--
ADT WO 9006045 A WO 1989-EP1419 19891121; EP 446260 A EP 1990-900184 19891121; JP 04501959 W WO 1989-EP1419 19891121, JP 1990-501005 19891121; AU 640626 B AU 1990-47586 19891121; EP 446260 B1 WO 1989-EP1419 19891121, EP 1990-900184 19891121; DE 68913555 E DE 1989-613555 19891121, WO 1989-EP1419 19891121, EP 1990-900184 19891121; US 5512439 A Cont of US 1991-688484 19910514, US 1994-272372 19940706; JP 3020271 B2 WO 1989-EP1419 19891121, JP 1990-501005 19891121; CA 2003508 C CA 1989-2003508 19891121
FDT JP 04501959 W Based on WO 9006045; AU 640626 B Previous Publ. AU 9047586, Based on WO 9006045; EP 446260 B1 Based on WO 9006045; DE 68913555 E Based on EP 446260, Based on WO 9006045; JP 3020271 B2 Previous Publ. JP

04501959, Based on WO 9006045
PRAI GB 1989-6643 19890322; GB 1988-27157 19881121; GB 1988-27158 19881121; GB 1988-27159 19881121; GB 1988-27160 19881121; GB 1988-27166 19881121; GB 1988-27167 19881121
REP NoSR.Pub; No-Citns.
IC **C12Q001-68**
ICM C12N015-11; **C12P019-34**; **C12Q001-68**
ICS C07K017-00; **C12N015-09**; C12N015-10; C12Q001-44; G01N033-553
AB WO 9006045 A UPAB: 20000524
Monodisperse, superparamagnetic particles carrying molecules of an oligonucleotide (I) are claimed. Also claimed is a method of immobilising a target nucleic acid (II) by contacting a soln. of (II) with the novel particles so that (I) hybridises to a nucleotide sequence on (II). Method of sequencing single-stranded nucleic acids comprises (a) preparing the novel particles carrying (I) (DNA or RNA) to be sequenced; (b) either (i) dividing the particles into 4 aliquots and adding to each aliquot a polymerase, mixed nucleoside triphosphates, a single dideoxynucleoside triphosphate, the latter being different for each aliquot and, if required a primer, at least one of the primer or nucleoside or dideoxynucleoside being labelled; or (ii) adding to all the particles a polymerase, mixed nucleoside triphosphates, 4 different dideoxynucleoside triphosphates each carrying a different label and, if required, a primer, thus synthesising a series of labelled DNA strands each having different chain lengths and ending with a particular dideoxy base; (c) liberating the labelled DNA strands and size fractionating them; and (d) determining the sequence. A kit is also provided.
USE/ADVANTAGE - The particles are useful as probes for hybridisation to (II) or for sequencing of (I). The probes carried by the particles react in the various reactions virtually as rapidly as if in soln. E.g. the total isolation of mRNA from a cell lysate using magnetic beads effected in about 15 mins. cf. 2 hrs. using an affinity column.
0/4
Dwg.0/4
FS CPI
FA AB
MC CPI: B04-B02C4; B04-B04A1; B05-A04; B11-C07B5; B11-C08; B12-K04A3; D05-H09; D05-H10; D05-H12
ABEQ EP 446260 B UPAB: 19940418
Monodisperse, superparamagnetic particles having a particle diameter standard deviation of less than 5%, said particles carrying a plurality of molecules of an oligonucleotide, each oligonucleotide comprising a section serving as a probe, said section being directly or indirectly attached via one end to a said particle.
Dwg.0/4
ABEQ US 5512439 A UPAB: 19960610
A plurality of monodisperse, superparamagnetic particles, where each particle comprises:
(i) superparamagnetic iron oxide dispersed within a polymer particle,
(ii) a coating which reduces **non specific binding**, and
(iii) a functional group carried by said coating for bonding a nucleic acid;
the particles are monodisperse and have a diameter standard deviation of less than 5%, and particles of said plurality carry a plurality of molecules of an oligonucleotide.
Dwg.0/4

L98 ANSWER 29 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1990-209565 [27] WPIX
CR 1990-209563 [27]; 1990-209564 [27]; 1990-209566 [27]
DNC C1990-090510
TI Prodn. of cDNA - by contacting liquid contg. mRNA with insol. support comprising magnetic particles.

DC B04 D16
IN HORNES, E; KORSNES, L
PA (DYNA-N) DYNAL AS; (HORN-I) HORNES E; (HOLM-I) HOLMES M J; (HORN-I) HORNES E
CYC 17
PI WO 9006044 A 19900614 (199027)* EN 35p
RW: AT BE CH DE ES FR GB IT LU NL SE
W: AU CH GB JP NO US
CA 2003500 A 19900521 (199031)
AU 9047585 A 19900626 (199038)
EP 444119 A 19910904 (199136)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04501958 W 19920409 (199221) 15p C12N015-10
EP 444119 B1 19950517 (199524) EN 18p C12P019-34 <--
R: AT BE CH DE ES FR GB IT LI LU NL SE
DE 68922743 E 19950622 (199530) C12P019-34 <--
US 5512439 A 19960430 (199623) 17p C12P019-34 <--
US 5759820 A 19980602 (199829) C12P019-34 <--
JP 2960776 B2 19991012 (199948) 13p C12N015-09 <--
CA 2003500 C 20000118 (200024) EN C12N015-10
CA 2003508 C 20000125 (200025) EN C12Q001-68 <--
ADT WO 9006044 A WO 1989-EP1418 19891121; JP 04501958 W WO 1989-EP1418 19891121, JP 1990-501004 19891121; EP 444119 B1 WO 1989-EP1418 19891121, EP 1990-900183 19891121; DE 68922743 E DE 1989-622743 19891121, WO 1989-EP1418 19891121, EP 1990-900183 19891121; US 5512439 A Cont of US 1991-688484 19910514, US 1994-272372 19940706; US 5759820 A Cont of WO 1989-EP1418 19891121, Cont of US 1991-688936 19910514, US 1994-280133 19940725; JP 2960776 B2 WO 1989-EP1418 19891121, JP 1990-501004 19891121; CA 2003500 C CA 1989-2003500 19891121; CA 2003508 C CA 1989-2003508 19891121
FDT JP 04501958 W Based on WO 9006044; EP 444119 B1 Based on WO 9006044; DE 68922743 E Based on EP 444119, Based on WO 9006044; JP 2960776 B2 Previous Publ. JP 04501958, Based on WO 9006044
PRAI GB 1988-27159 19881121; GB 1988-27158 19881121; GB 1988-27157 19881121; GB 1988-27160 19881121; GB 1988-27166 19881121; GB 1988-27167 19881121; GB 1989-6643 19890322
REP NoSR.Pub; 1.Jnl.Ref; EP 184056; EP 223618; EP 265244; EP 288737; WO 8504674; WO 8807585
IC ICM **C12N015-09**; C12N015-10; **C12P019-34**; **C12Q001-68**
ICS B01J019-08; C07H021-04; C12N015-00; C12N015-11; C12Q001-70; G01N033-553
AB WO 9006044 A UPAB: 20000524
Prodn. of cDNA involves (a) contacting a liquid contg. mRNA with an insol. support having DNA probes attached to it by their 5' termini, where the mRNA is hybridised to the probes and hence to the support; (b) removing the liquid; and (c) adding enzymes and nucleotides in soln. so that the probe functions as a primer to produce single strand (ss) cDNA on the RNA templates.
ADVANTAGE - The method is rapid and simple and avoids the prior art problems of loss of mRNA by hydrolysis and degradation and sepn. of excess linker reagent.
0/0
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-B02C; B04-B03B; B04-B04A1; D05-H12
ABEQ EP 444119 B UPAB: 19950626
A process for the production of cDNA which includes the steps of: (a) contacting a liquid containing mRNA with an insoluble support having DNA probes attaached thereto via the 5'-terminus thereof whereby the mRNA is hybridised to said probes and hence to said support; (b) removing said liquid; and (c) adding enzymes and nucleotides in solution whereby the

probe functions as a primer to produce single stranded cDNA on the mRNA templates.
Dwg.0/0

ABEQ US 5512439 A UPAB: 19960610
A plurality of monodisperse, superparamagnetic particles, where each particle comprises:
(i) superparamagnetic iron oxide dispersed within a polymer particle,
(ii) a coating which reduces **non specific binding**, and
(iii) a functional group carried by said coating for bonding a nucleic acid;
the particles are monodisperse and have a diameter standard deviation of less than 5%, and particles of said plurality carry a plurality of molecules of an oligonucleotide.
Dwg.0/4

L98 ANSWER 30 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1989-309546 [42] WPIX
CR 1989-192704 [26]
DNC C1989-137062
TI Detection of nucleic acid sequences - based on their activity as co factors in catalytic reactions in which complementary labelled probe is cleaved.
DC B04 D16
IN WALDER, J A; WALDER, R Y
PA (IOWA) UNIV IOWA STATE RES FOUND INC; (UNIP) UNIV IOWA
CYC 14
PI WO 8909284 A 19891005 (198942)* EN 63p
RW: AT BE CH DE FR GB IT LI LU NL SE
W: AU JP
AU 8932944 A 19891016 (199008)
EP 365627 A 19900502 (199018)
R: AT BE CH DE FR GB IT LI LU NL SE
JP 02503515 W 19901025 (199049)
EP 365627 B1 19931222 (199351) EN 31p C12Q001-68 <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 68911648 E 19940203 (199406) C12Q001-68 <--
EP 365627 A4 19901010 (199513)
US 5403711 A 19950404 (199519) 19p C12Q001-68 <--
JP 2856804 B2 19990210 (199911) 24p C12Q001-68 <--
ADT WO 8909284 A WO 1989-US1025 19890313; EP 365627 A EP 1989-903936 19890313; JP 02503515 W JP 1989-503541 19890313; EP 365627 B1 EP 1989-903936 19890313, WO 1989-US1025 19890313; DE 68911648 E DE 1989-611648 19890313, EP 1989-903936 19890313, WO 1989-US1025 19890313; EP 365627 A4 EP 1989-903936 ; US 5403711 A CIP of US 1987-126564 19871130, Cont of US 1988-173127 19880324, Cont of US 1991-757555 19910911, US 1993-88622 19930706; JP 2856804 B2 JP 1989-503541 19890313, WO 1989-US1025 19890313
FDT EP 365627 B1 Based on WO 8909284; DE 68911648 E Based on EP 365627, Based on WO 8909284; JP 2856804 B2 Previous Publ. JP 02503515, Based on WO 8909284
PRAI US 1988-173127 19880324; US 1987-126564 19871130; US 1991-757555 19910911; US 1993-88622 19930706
REP US 4683195; US 4683202; US 4800159; EP 185494; EP 227976; EP 246864
IC **C12Q001-68**
ICM **C12Q001-68**
ICS C07H021-04; **C12N015-09; C12P019-34**
AB WO 8909284 A UPAB: 19970926
(A) Detection of nucleic acid (NA) sequences which serve as a cofactor for a catalytic reaction in which a complementary labelled NA probe is cleaved and detected; comprises (a) hybridising of a target sequence to a labelled NA probe to provide a probe:target sequence duplex, (b) cleaving of the labelled probe within the probe-target sequence duplex to release the target sequence intact, (c) recycling of the target sequence

repeatedly through the reaction pathway and (d) detecting the extend of cleavage of the labelled probe; the labelled probe may be attached to a solid support during the hybridisation and cleavage reaction and cleaved fragments bearing the reporter gp. may be released into soln; the solid support may be latex, polystyrene, crosslinked dextran or glass beads, cellulose, or a teflon or nylon membrane; cleavage of the labelled probe may be mediated by an enzyme or other catalyst with RNaseH activity and **nonspecific** cleavage suppressed by the use of single-stranded ribonuclease inhibitors such as vanadate, RNAsin or Inhibit-ACE.

USE/ADVANTAGE - The method allows sensitive detection of specific NA sequences in biological and clinical samples. Recycling of the target through the reaction pathway enables it to capture many molecules of the probe, leading to a large increase in the sensitivity of the assay.

FS CPI
FA AB
MC CPI: B04-B02B3; B04-B04A1; B11-C07; B11-C08D1; B12-K04; D05-H12
ABEQ EP 365627 B UPAB: 19940209
A method of detecting nucleic acid sequences in which the sequences serve as a cofactor for a catalytic reaction in which a complementary labelled nucleic acid probe is cleaved and detected the method comprising hybridising of a target sequence to a labelled nucleic acid probe to provide a probe, target sequence duplex, cleaving the labelled probe within the probe target sequence duplex to release the target sequence intact, recycling of the target sequence repeatedly through the reaction pathway, and detecting the extent of cleavage of the labelled probe.
Dwg.0/5C
ABEQ US 5403711 A UPAB: 19950524
Detection of a target nucleic acid target sequence comprises hybridisation of a test sample with a labelled nucleic acid probe; cleavage of the labelled probe with an enzyme that leaves the target sequence intact; repetition of these steps, recycling the target sequence; and detection of the cleaved label function to confirm the presence of the target sequence.

USE - The process facilitates the detection of specific sequences.

ADVANTAGE - The recycling steps give rise to a more intense marker signal.
Dwg.0/5

L98 ANSWER 31 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1989-242804 [34] WPIX
CR 1988-114361 [17]; 1998-129863 [12]; 1998-296758 [26]
DNN N1989-185084 DNC C1989-108068
TI Assays for target polynucleotide(s) - by isolation from extraneous non-target polynucleotide(s) and impurities and amplification.
DC B04 D16 J04 S03
IN COLLINS, M L; HALBERT, D N; KING, W; LAWRIE, J M
PA (STAD) AMOCO CORP
CYC 13
PI EP 328829 A 19890823 (198934)* EN 35p
R: AT BE CH DE FR GB IT LI LU NL SE
AU 8827359 A 19890713 (198935)
JP 01211500 A 19890824 (198940)
EP 328829 B1 19950913 (199541) EN 38p C12Q001-68 <--
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3854470 G 19951019 (199547) C12Q001-68 <--
JP 2817926 B2 19981030 (199848) 31p C12Q001-68 <--
ADT EP 328829 A EP 1988-312135 19881221; JP 01211500 A JP 1988-323183 19881221; EP 328829 B1 EP 1988-312135 19881221; DE 3854470 G DE 1988-3854470 19881221, EP 1988-312135 19881221; JP 2817926 B2 JP 1988-323183 19881221
FDT DE 3854470 G Based on EP 328829; JP 2817926 B2 Previous Publ. JP 01211500
PRAI US 1987-136920 19871221
REP A3...9038; EP 154505; EP 159719; EP 200362; EP 265244; No-SR.Pub; WO 8605815; WO 8701730; EP 184056

IC C07H021-00; C12N015-00; **C12P019-34**; **C12Q001-68**; G01N033-54
ICM **C12Q001-68**
ICS **C12N015-09**; **C12P019-34**; C12Q001-00; G01N033-50; G01N033-53; G01N033-54; G01N033-543
ICA C07H021-00; C12N015-00
AB EP 328829 A UPAB: 19980701
A method of amplification of target polynucleotide molecules potentially contained in a sample with non-target polynucleotides comprises (A) (a) contacting the sample with a support capable of specifically associating with the target under **binding** conditions, (b) sepg. the support from the remaining sample to form a removal prod. which in the presence of target includes target, (c) subjecting the removal prod. to amplification which in the presence of target forms an amplification prod. or (b) (a) contacting the sample with a polynucleotide probe under **binding** conditions to form a probe-target complex, (b) sepg. the probe from the non-target polynucleotides in the sample to form a removal prod. which in the presence of target includes the probe-target complex, (c) subjecting the removal prod. to amplification to form an amplification prod. the generation of which is dependent on the presence of target. The amplifying step may comprise treating the target with a polymerase, e.g. RNA polymerase, Q beta replicase, transcriptase or DNA polymerase,. Prior to treting the target with the polymerase, the target may be caused to replicate using DNA polymerase and **non-specific** oligonucleotide primer.
USE/ADVANTAGE - The methods provide rapid, sensitive detection of nucleic acid targets in clinical samples adaptable to non-radioactive labelling techniques and automation.
FS CPI EPI
FA AB; DCN
MC CPI: B04-B02C4; B04-B04A1; B12-K04A; D05-A02B; D05-H12; J04-B01
EPI: S03-E14H4
ABEQ EP 328829 B UPAB: 19951019
A method of amplification of a target polynucleotide molecule potentially contained in a sample with non-target polynucleotides comprising the steps of (a) contacting the sample potentially contg. the target with a first support and a first probe capable of specifically associating with the target under **binding** conditions and further capable of associating with the first support under **binding** conditions, (b) sepg. the first support from the remaining sample to form a removal prod. which in the presence of target includes the target, (c) subjecting the removal prod. to amplification which in the presence of target forms an amplification prod.
Dwg.8/8

L98 ANSWER 32 OF 32 WPIX (C) 2003 THOMSON DERWENT
AN 1989-194038 [27] WPIX
CR 1999-174359 [15]
DNC C1989-085749
TI Nucleic acid hybridisation carrier - having a single stranded polynucleotide immobilised by a peptide bond on a non-porous organic polymer particle.
DC B04 D16 J04
IN FURUICHI, Y; HIKATA, M; KURIBAYASHI, K; KURIBAYASH, K
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) HOFFMANN-LA ROCHE AG; (JAPS) JAPAN SYNTHETIC RUBBER CO LTD; (JAPS) JSR CORP
CYC 10
PI EP 322677 A 19890705 (198927)* EN 14p
R: CH DE FR GB IT LI NL
JP 01171499 A 19890706 (198933)
EP 322677 B1 19940810 (199431) EN 14p C07H021-04
R: CH DE FR GB IT LI NL
DE 3851045 G 19940915 (199436) C07H021-04

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     CA 1334385    C  19950214 (199514)              C07H021-04
     JP 08004519   B2 19960124 (199608)        9p    C12Q001-68      <--
     JP 2880996    B2 19990412 (199920)       10p    C12Q001-68      <--
     US 5972611    A  19991026 (199952)              C12Q001-68      <--
ADT  EP 322677 A EP 1988-121070 19881216; JP 01171499 A JP 1987-329402
     19871225; EP 322677 B1 EP 1988-121070 19881216; DE 3851045 G DE
     1988-3851045 19881216, EP 1988-121070 19881216; CA 1334385 C CA
     1988-587011 19881223; JP 08004519 B2 JP 1987-329402 19871225; JP 2880996
     B2 Div ex JP 1987-329402 19871225, JP 1998-102199 19871225; US 5972611 A
     Cont of US 1988-288601 19881222, Cont of US 1991-674284 19910321, Cont of
     US 1992-888409 19920521, Cont of US 1993-3904 19930113, Cont of US
     1995-437910 19950510, Cont of US 1996-662830 19960612, US 1997-964448
     19971104
FDT  DE 3851045 G Based on EP 322677; JP 08004519 B2 Based on JP 01171499; JP
     2880996 B2 Previous Publ. JP 11028100
PRAI JP 1987-329402   19871225; JP 1998-102199   19871225
REP  1.Jnl.Ref; A3...9119; EP 101985; EP 180945; No-SR.Pub
IC   C07H021-04; C12N015-00; C12Q001-68
     ICM  C07H021-04; C12Q001-68
     ICS  C07H021-02; C12N015-00; C12N015-09; C12P019-34;
          C12Q001-00
AB   EP    322677 A UPAB: 19991210
     A hybridisation carrier is claimed characterised in that a single stranded
     polynucleotide of formula 5'-(dN)n(dT)m-3' (I) is immobilised by a peptide
     bond on a non-porous surface of an organic polymer particle of 0.05-5
     micrometers dia. (N = adenine, guanine or cytosine; T = thymine; n = an
     integer of 2 or larger; m = an integer of 5 or larger).
          USE/ADVANTAGE - The hybridisation carrier is useful for the
     detection, isolation and purificn. of nucleic acid contg. a specific base
     sequence and hardly causes any nonspecific trapping of nucleic
     acid or other trouble in the hybridisation to enable the highly accurate
     detection, isolation and purificn. In addn. the hybridisation carrier can
     be used for cDNA synthesis.
     Dwg.0/2
FS   CPI
FA   AB
MC   CPI: B04-B04A1; B12-K04; D05-H10; D05-H12; J04-B01B
ABEQ EP    322677 B UPAB: 19940921
     A hybridization carrier which is characterized in that a single stranded
     polynucleotide represented by the following formula 5'-(dN)n(dT)m-3'
     wherein N represents adenine, guanine or cytosine, T represents thymine, n
     is an integer of 2 or larger, and m is an integer of 5 or larger, is
     immobilized by means of the peptide bond, on a non-porous surface of an
     organic polymer particle having 0.05-5 um in diameter.
     Dwg.02


=> d his

     (FILE 'HOME' ENTERED AT 14:23:12 ON 13 JAN 2003)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 14:23:46 ON 13 JAN 2003
               E WO99-US8745/AP,PRN
L1           1 S E3,E4
               E US98-63311/AP,PRN
L2           1 S E4
               E US2001049108/PN
L3           1 S E3
L4           1 S L1-L3
               E AFFYMETRIX/PA,CS
L5         213 S E3-E27
               E MCGALL G/AU
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L6            72 S E3-E9
                 E MC GALL G/AU
                 E GOLDBERG M/AU
L7           746 S E3-E20,E44-E51
                 E GOLDBERT M/AU
L8             2 S E4,E5
                 E RYDER T/AU
L9            42 S E3,E5,E7-E9,E17
                 E WOODMAN S/AU
L10            6 S E3,E4,E6,E7
L11            1 S L4 AND L5-L10
L12           56 S L5 AND L6-L10
L13           11 S L6 AND L7-L10
L14            3 S L7,L8 AND L9,L10
L15            1 S L9 AND L10
L16           12 S L13-L15
                 SEL RN L4

     FILE 'REGISTRY' ENTERED AT 14:35:50 ON 13 JAN 2003
L17           14 S E1-E14
L18           12 S L17 NOT SQL/FA
L19            6 S L18 NOT P/ELS
L20            5 S L19 NOT OC4/ES
L21              STR
L22           50 S L21
L23         5732 S L21 FUL
                 SAV L23 BORIN862/A
L24            4 S L17 AND L23
L25              STR L21
L26            2 S L25 SAM SUB=L23
L27            8 S L25 FUL SUB=L23
                 SAV L27 BORIN862A/A
L28              STR L26
L29            0 S L28 SAM SUB=L23
L30              STR L28
L31            1 S L30 SAM SUB=L23
L32            6 S L30 FUL SUB=L23
                 SAV L32 BORIN862B/A
L33            2 S L27 AND L32
L34            4 S L32 NOT B/ELS
L35            4 S L33,L34
L36              STR L21
L37           50 S L36 SAM SUB=L23
L38         5724 S L23 NOT L24,L35

     FILE 'HCAPLUS' ENTERED AT 14:54:07 ON 13 JAN 2003
L39           19 S L35
L40           33 S L24
L41           49 S L39,L40
L42            2 S L5-L10 AND L41
L43         3536 S L38
L44           11 S L5-L10 AND L43
L45           12 S L42,L44
L46            1 S L20 AND L45
                 E LANGMUIR/CT
                 E E11+ALL
L47         5878 S E3,E2+NT
                 E GLASS/CT
L48          650 S GLASS/CW (L) FUNCTIONAL?
                 E GLASS, USE/CT
L49           52 S E4 (L) FUNCTIONAL?
                 E METAL OXIDE/CT
                 E E5+ALL
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                E METAL OXIDES/CT
                E E3+ALL
L50         14912 S E2
L51             4 S L41,L43 AND L47-L50
L52             5 S L42,L46,L51
                E PROTECT/CT
L53          6368 S E23,E24
                E E24+ALL
L54          6605 S E3,E2+NT
L55           228 S L41,L43 AND L54
L56             9 S GENETIC?/SC,SX AND L55
                E NUCLEIC ACID HYBRIDIZATION/CT
                E E3+ALL
L57        227686 S E1+NT
L58        576289 S E11+NT OR E13+NT OR E14+NT
L59        153377 S E10+NT
                E OLIGO/CT
                E OLIGONUC/CT
                E E10+ALL
L60         52170 S E9,E8+NT
L61          2553 S L41,L43 AND L57-L60
L62           184 S L61 AND L55
L63          2194 S L20,L47-L50 AND L57-L60
L64            15 S L63 AND L53,L54
L65             1 S L41,L42 AND (NONSPECIFIC OR NON SPECIFIC)(L)BIND?
L66            13 S L52,L56,L65
L67             1 S L65 AND L66
L68            13 S L66,L67
L69            14 S L64 NOT L68
L70            46 S L41 NOT L68
L71             2 S L41,L42 AND (NONSPECIF? OR NON SPECIF?)
L72            14 S L68,L71
L73            45 S L41 NOT L72
                  SEL DN AN 5 40 45
L74             3 S L73 AND E1-E9
L75            17 S L72,L74
L76           223 S L5-L10 AND L57-L60
L77            28 S L76 AND ?BIND?
                  SEL DN AN 1 10 14 15 18
L78             5 S L77 AND E10-E24
L79            22 S L75,L78
L80            22 S L77 NOT L79
                  SEL DN AN 16
L81             1 S E25-E27 AND L80
L82            23 S L79,L81
L83             4 S L82 AND (UV OR ULTRAVIOL? OR LIGHT)
L84            23 S L82,L83

     FILE 'REGISTRY' ENTERED AT 15:53:55 ON 13 JAN 2003

     FILE 'HCAPLUS' ENTERED AT 15:54:51 ON 13 JAN 2003
L85            23 S L84 OR L4

     FILE 'HCAPLUS' ENTERED AT 15:55:11 ON 13 JAN 2003

     FILE 'WPIX' ENTERED AT 15:56:06 ON 13 JAN 2003
                E US200100491008/PN
                E WO99-US8745/AP,PRN
L86             1 S E3
L87         24240 S C12Q001-68/IC,ICM
L88          7095 S C12N015-09/IC,ICM,ICS AND L87
L89           126 S L88 AND (NONSPECIF? OR NON SPECIF?)/BIX
L90            41 S L89 AND C12P019/IC,ICM,ICS
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L91          15 S L90 AND (BIND? OR BOUND?)
L92           9 S L91 NOT (SELEX OR NEOPLASIA OR LUNG OR PROTEIN OR CYCLING)/TI
L93           9 S L86,L92
L94          26 S L90 NOT L91,L93
                SEL DN AN 2 6 7 8 9 10 12 13 14 16 17 20 21 22 23 25 26
L95           9 S L94 NOT E1-E35
L96          17 S L94 NOT L95
                SEL DN AN 8 9 13
L97          14 S L96 NOT E36-E41
L98          32 S L93,L95,L97

     FILE 'WPIX' ENTERED AT 16:11:23 ON 13 JAN 2003
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